Dissertation on

"CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE"

Submitted in partial fulfillment for the Degree of

M.D GENERAL MEDICINE

BRANCH – I

THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

INSTITUE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI – 600003

APRIL 2017

CERTIFICATE

This is to certify that the dissertation titled "**CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE**" is the bonafide original work done by **DR. DIANA. G**, post graduate student, Institute of Internal medicine, Madras medical college, Chennai-3, in partial fulfillment of the University Rules and Regulations for the award of MD Branch -1 General Medicine, under our guidance and supervision, during the academic year 2014-2017.

Prof. S.MAYILVAHANAN M.D.,
Director & Professor,
Institute of Internal Medicine,
Madras Medical College &
RGGGH, Chennai – 600003.

Prof.K.S.CHENTHIL M.D.,
Professor of Medicine,
Institute of Internal Medicine,
Madras Medical College &
RGGGH, Chennai – 600003.

Prof. M.K.MURALITHARAN M.S,M.ch,
DEAN,
Madras Medical College & Rajiv Gandhi Government General Hospital,
Chennai 600 003.

DECLARATION

I, **Dr. DIANA G** solemnly declare that dissertation titled "**CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE**" is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during March 2016 to August 2016 under the guidance and supervision of my unit chief **Prof. K.S.CHENTHIL M.D**, Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH-I**.

Place: Chennai -03
Date:

Dr. DIANA G
MD General Medicine,
Post Graduate,
Institute of Internal Medicine,
Madras Medical College,
Chennai - 03

ACKNOWLEDGEMENT

I owe my thanks to Dean, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3. **Prof.M.K.MURALITHARAN, M.S., M.ch** for allowing me to avail the facilities needed for my dissertation work.

I am grateful to beloved mentor **Prof. S.MAYILVAHANAN** M.D., Director and Professor, Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-03 for permitting me to do the study and for his encouragement.

With extreme gratitude, I express my indebtedness to my beloved Chief and teacher **Prof. K.S.CHENTHIL M.D,** for his motivation, advice and valuable criticism, which enabled me to complete this work.

I am extremely thankful to my Assistant Professor **Dr.PRIYADHARSHINI, M.D.,** and **Dr.BIJIN OLIVER JOHN. M.D.,** for their guidance and encouragement.

I am also thankful to all my unit colleagues and other post graduates in our institute for helping me in this study and my sincere thanks to all the patients and their families who were co-operative during the course of this study.

ABBREVIATIONS

NIHSS	-	National Institute of Health Stroke Scale
MRS	-	Modified Rankin Scale
MCA	-	Middle Cerebral Artery
CT	-	Computed Tomography
MRI	-	Magnetic Resonance Imaging
ICA	-	Internal Carotid Artery
PICA	-	Posterior Inferior Cerebellar Artery
AICA	-	Anterior Inferior Cerebellar Artery
TIA	-	Transient Ischemic Attack
SAH	-	Subarachnoid Hemorrhage
ICH	-	Intra Cerebral Hemorrhage
AF	-	Atrial Fibrillation
CCF	-	Congestive Cardiac Failure
TACS	-	Total Anterior Circulation Stroke
MAP	-	Mean Arterial Pressure
MPT	-	Mitochondrial permeability Transition
CVA	-	Cerebro vascular accident
OCP	-	Oral Contraceptive Pills
PCA	-	Posterior Cerebral Artery
ICT	-	Intracranial Tension

ACA	-	Anterior Cerebral Artery
IHD	-	Ischemic heart disease
DCM	-	Dilated cardiomyopathy
rtPA	-	Recombinant Tissue Plasminogen Activator
PAN	-	Polyarteritis Nodosa
POCS	-	Posterior Circulation Stroke
LACS	-	Lacunar stroke
PACS	-	Partial anterior circulation stroke

CONTENTS

INTRODUCTION

INTRODUCTION

Stroke has now become the second leading cause of death worldwide.[13] Stroke is an important cause for prolonged disability.[1] Given this immense burden that stroke exerts, there becomes the need to develop more precise estimates of a stroke survivors prognosis and it remains an very important goal. And also identification of predictors of mortality is very vital so that we can institute many prompt therapeutic measures to improve outcome.

Serum calcium levels play a very significant role in the molecular pathway involving ischemic neuronal death and damage. Calcium has been studied with relationship to stroke risk factors and stroke incidence.[27]It has been demonstrated in many studies that calcium levels are seen decreased in cerebral ischemia. Usually cerebral ischemia causes shifting of calcium from extracellular space to intracellular compartment. This intracellular calcium accumulated leads to neuronal damage by triggering cytotoxic events.

Serum albumin acts as a unique multifunctional protein and it has many neuroprotective effects. [30] There is many growing evidence of its prognostic significance in acute ischemic stroke.[32]

Albumin has many intravascular effects. It decreases erythrocyte sedimentation under conditions of no flow. Albumin acts as a important antioxidant agent. Its one of the neuroprotective property is the antagonism of stagnation, thrombosis, and adhesion of leucocytes within postcapillary microcirculation.

This study to determine the prognostic value of serum calcium and serum albumin in predicting the severity and functional outcome in patients of acute ischemic stroke.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVE

To study the corrected serum calcium and serum albumin in acute ischemic stroke.

To assess the role of corrected serum calcium and serum albumin in predicting the severity and short term functional outcome in acute ischemic stroke using NIHSS and modified rankin scale.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Before several centuries, Hippocrates describes stroke as apoplexy means – “thunder struck ,sudden depriving of one’s sense”. He said people of ages between 40-60 are at more risk when compared to other fellow person.[1] In AD 131,Galen based on his dissections of animals, was first person to describe the structure of the brain and its anatomy and blood supply.

Johann Jacob Wepfer (1620- 1695) dissected corpses in the morgue and pinpointed that the sudden onset of this apoplexy is due to disruption of blood supply to brain. He said that apart from occlusion of the vessels, bleeding from the vessels in the brain was an important cause of this apoplexy.[1]He was the first person to clearly differentiate between ischemic and hemorrhagic stroke.

Thomas Wills (1621-1675), a neuro-anatomist proposed about the cerebral blood vessel anastomoses at the base of brain(CEREBRAL ANASTOME), and it was named after him – CIRCLE OF WILLIS. He too describes transient ischemicattacks and existence of occlusion of carotid artery, the embolus as etiology for stroke.

John Abercrombie published paper on this apoplexy and he pointed headache, stupor, paralysis are the features of apoplexy.[1] Following this,several studies were done and different other stroke syndromes were established. During 20th century, there were several advanced technology allowing better visualization about the brain anatomy and their functions, and about the pathological lesions affecting the brain.

Antonio Egas Moniz (1874-1955), a neurosurgeon,developer of cerebral angiography. He surgically exposed and ligated cranial artery in neck, then 30% sodium iodide was injected and then skull films were taken at regular intervals. Seldinger, from Sweden, introduced modern angiography, in which a small catheter was introduced into artery over flexible guide wire after withdrawing the needle.

In 1960, Hounsfield from Britain, introduced the concept of Computed Tomography (CT). About mid 1980, MRI proved to be superior to CT in picking up the old hemosiderin containing hemorrhages, lesion in posterior cranial fossa,vascular malformation, lesion abutting on bony surfaces.

Franklin, in 1961, pointed the uses of ultrasound in imaging the extra cranial carotid vessels. About the end of 20th century, advanced imaging technique with CT, MRI spectroscopy helped in the localisations, severity and potential reversibility of cerebral ischemia.

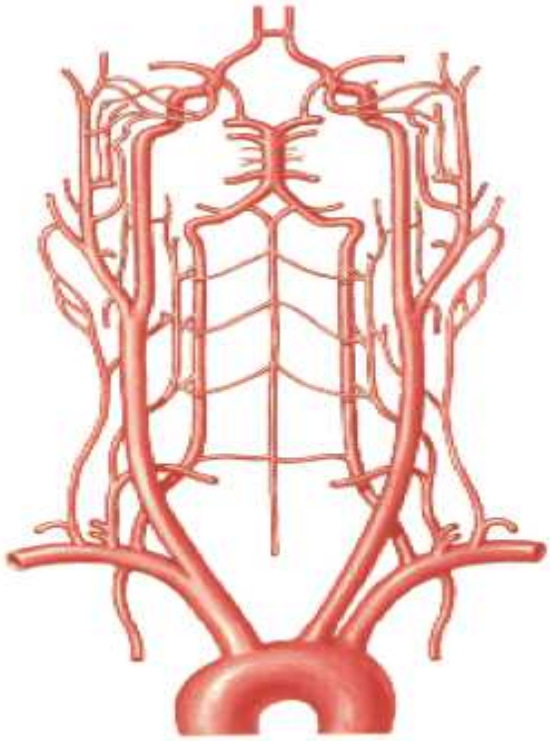
Vascular lesions can be visualised better by CT and MR angiography.[1,2] These advancement will help in better management of the stroke in upcoming future.

BLOOD SUPPLY OF BRAIN

Brain is supplied by

Internal carotid artery

Vertebral artery



Internal carotid arteries

They arises from common carotid arteries and enter middle cranial fossa through the carotid canal which opens in the side of foramen lacerum .It turns upwards to reach the side of body of sphenoid bone.It

then turns forward in the cavernous sinus to reach the medial aspect of anterior clinoid process and lies lateral to optic chiasma. Its course follows a series of bends (carotid siphon).

BRANCHES

Hypophyseal arteries

Ophthalmic artery

Anterior choroidal artery

Anterior cerebral artery

Posterior communicating artery

Middle cerebral artery

Ophthalmic artery is first branch from internal carotid artery, which supplies eye and other structures in the orbit.

Posterior communicating artery is the next branch, and it runs back to join the posterior cerebral artery, and supplying optic chiasma, optic tract, hypothalamus, midbrain, thalamus.

Anterior choroidal artery - which arises from distal region of ICA and it supplies the internal capsule, basal ganglia, thalamus, lateral geniculate body, optic tract, midbrain, proximal optic radiation.

Middle cerebral artery- it enters sylvian fissure, before it enters it gives deep cerebral branches (Lenticulostriate branches). The middle

cerebral artery, in the sylvian fissure, divides into superior & inferior division and supplies the lateral part of the cerebral cortex. The lenticulostriate branches supply the, internal capsule (posterior limb), putamen and outer globus pallidus.

Anterior cerebral artery –it passes medially above the optic nerve and then passes in to the great longitudinal fissure between the frontal lobe where it joins the corresponding vessels of the opposite side by anterior communicating artery. It follows the curvature of corpus callosum and ramifies over medial surface of frontal and parietal lobe and supply them.Also supply a narrow lateral band of frontal and parietal cortices.The territory supplied by it includes motor sensory cortices for the lower limb.

VERTEBRAL ARTERY

Vertebral artery arises from the first part of subclavian artery, then ascends through the transverse foramina of upper 6 cervical vertebrae, then it join with the vertebral artery of the other side to form basilar artery. Its branches includes – anterior spinal artery, posterior spinal artery, PICA (posterior inferior cerebellar artery), small penetrating branches to medulla. PICA supplies inferior vermis, inferior and posterior surfaces of the cerebellum, brainstem.

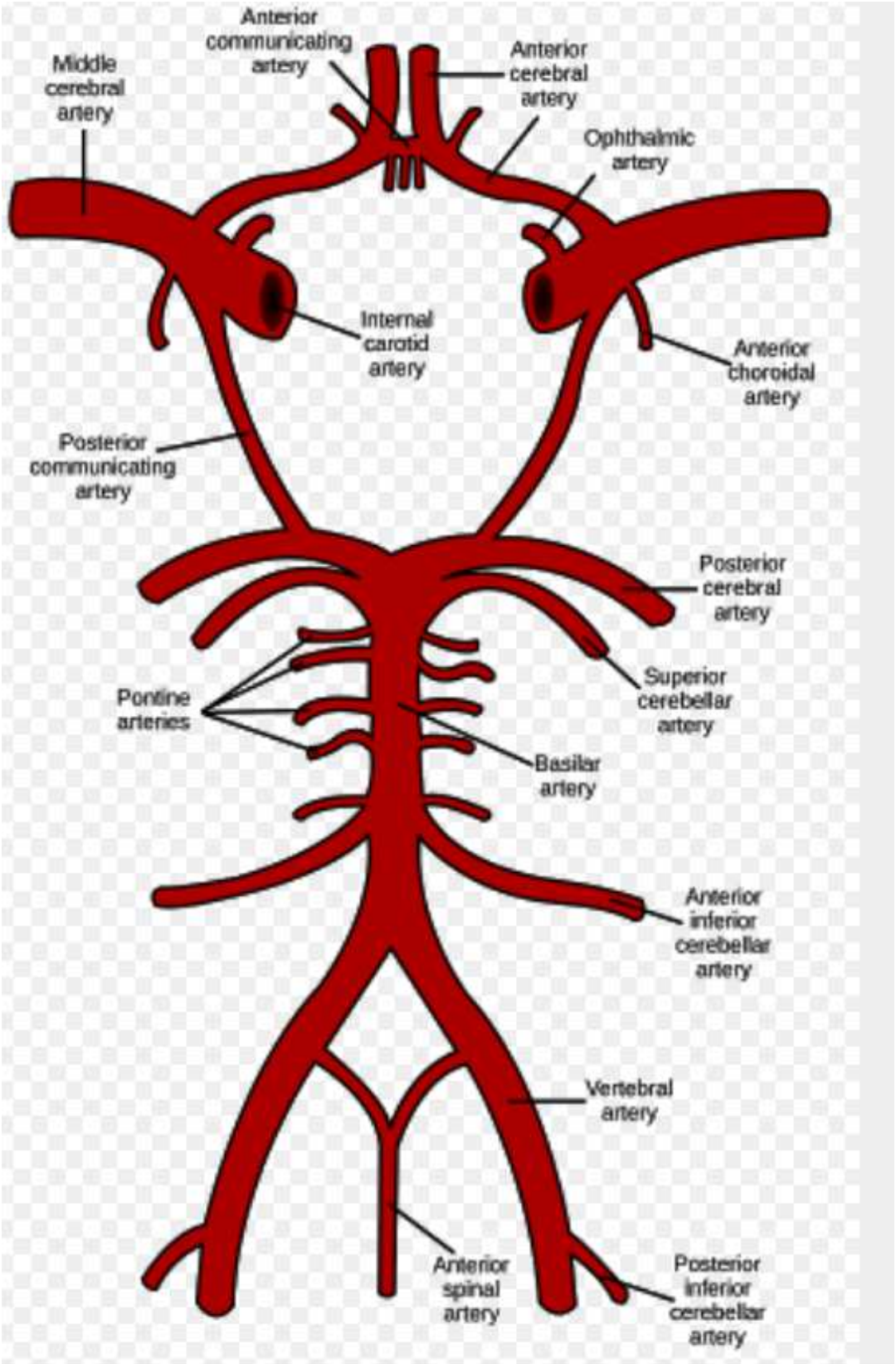
Basilar artery ascends to the pons and in the inter-peduncular cistern and it divides into posterior cerebral artery. The other branches of it are

- Labyrinthine artery
- AICA (anterior inferior cerebellar artery) which supply the rostral cerebellum, brainstem, inner ear
- the superior cerebellar artery ,supplying the brainstem, cerebellar hemisphere(superior part) ,vermis, dentate nucleus
- posterior cerebral artery.

The posterior cerebral artery, which winds around the midbrain near the occulomotor nerve. It supplies temporal lobe (inferior part), occipital lobe. Its deep branches supply mainly midbrain, thalamus, hypothalamus, and geniculate bodies (thalamostriate branches).

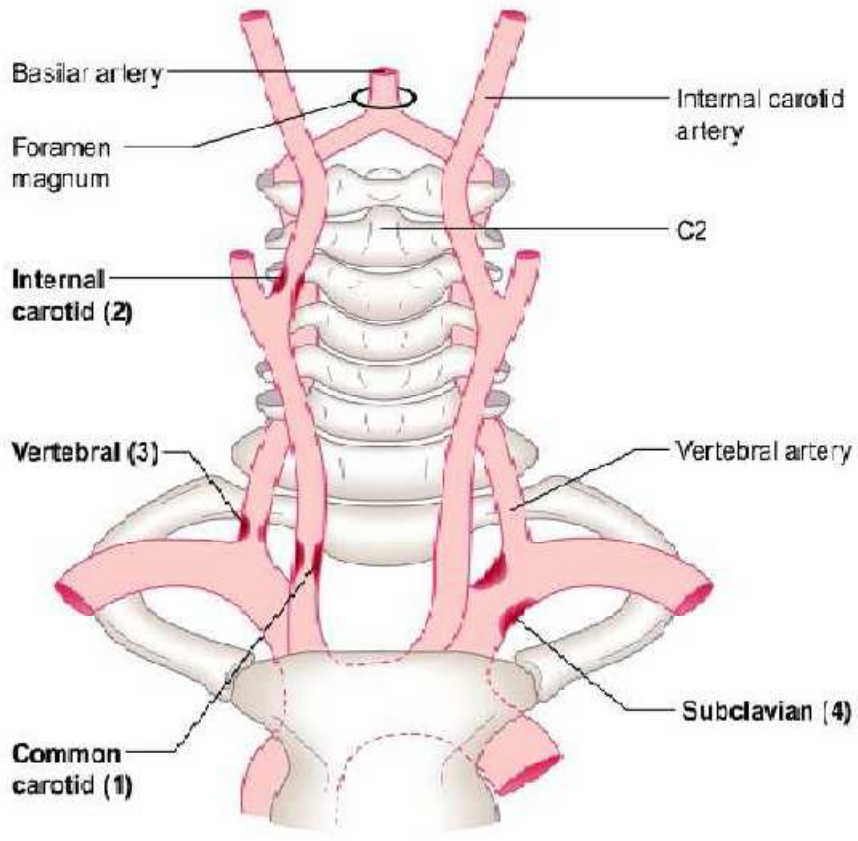
CIRCLE OF WILLIS

It is an arterial anastomosis in the interpeduncular fossa, formed anteriorly by two ACA (anterior cerebral artery), which is connected by anterior communicating artery anteriorly, posteriorly by two PCA (posterior cerebral artery), communicating with anterior circulation by the posterior communicating artery.


Anterior communicating artery
Middle cerebral artery
Anterior cerebral artery
Ophthalmic artery
Internal carotid artery
Anterior choroidal artery
Posterior communicating artery
Posterior cerebral artery
Superior cerebellar artery
Pontine arteries
Basilar artery
Anterior inferior cerebellar artery
Vertebral artery
Anterior spinal artery
Posterior inferior cerebellar artery

COLLATERAL BLOOD SUPPLY IN THE BRAIN

Usually the anterior two-third of the cerebral circulation is by the internal carotid artery and the posterior one – third is by vertebral artery. In blood vessels occlusion, collateral develop distal to the site of occlusion. collateral development depends on the vessels occluded, and also whether other artery are free of disease or not.



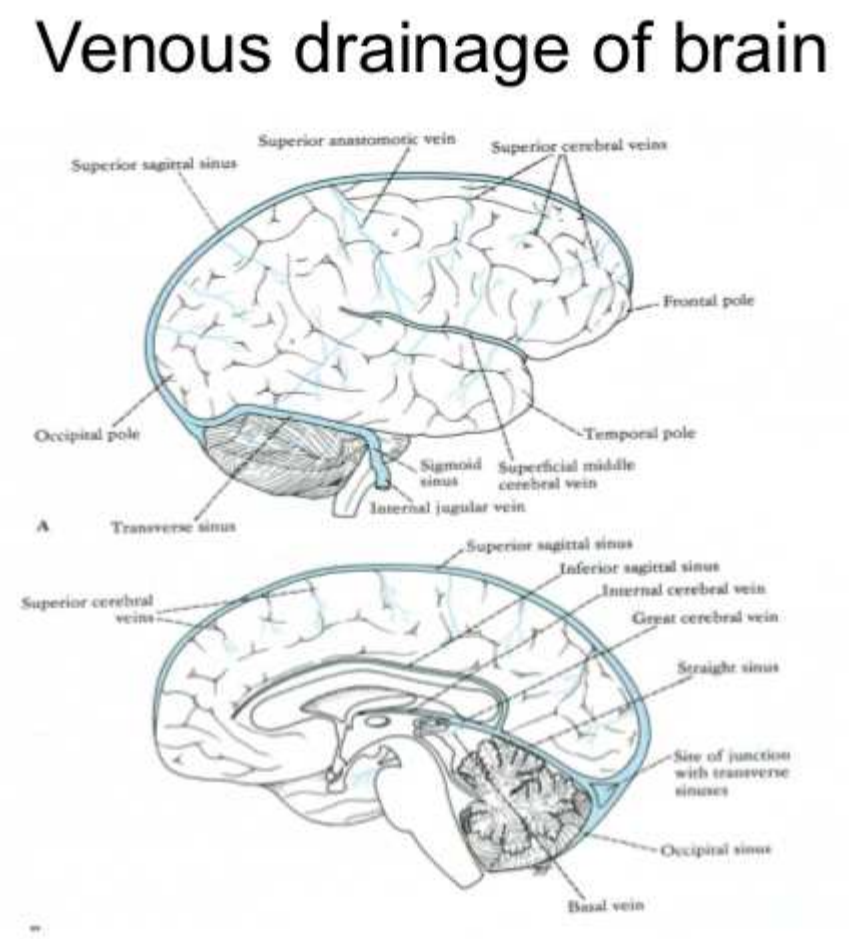
Principal sites of stenoses in extracerebral arteries (shown in bold, 1 to 4).

Venous drainage of the brain

1. Superficial cerebral veins

2 Deep cerebral veins

Both these veins drains into the dural venous sinuses. It further drains into the internal jugular vein. The cerebral veins are valveless and they are thin walled, & the blood flow in these veins are in the same direction as that of nearby arteries.[4]



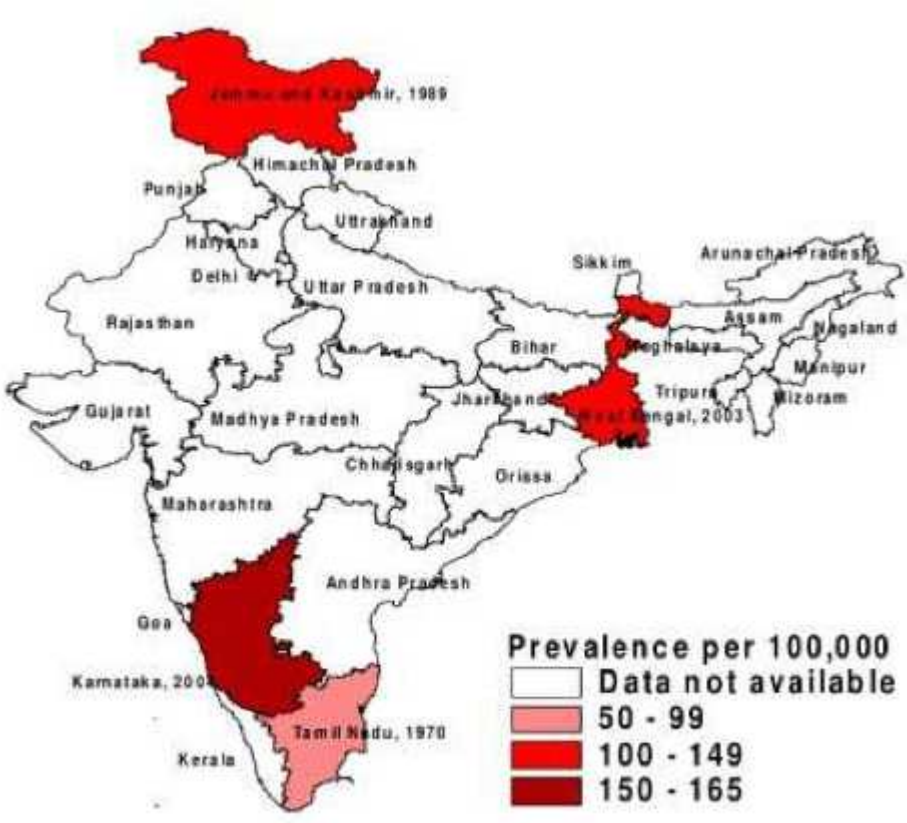
EPIDEMIOLOGY OF THE STROKE

PREVALENCE OF STROKE

The first community based study of stroke was carried out in vellore between 1968 and 1969. Second one was in Rohtak during 1971-1974.There is 38% increase in stroke among women from year 1975-78 and 1983-85.[7]

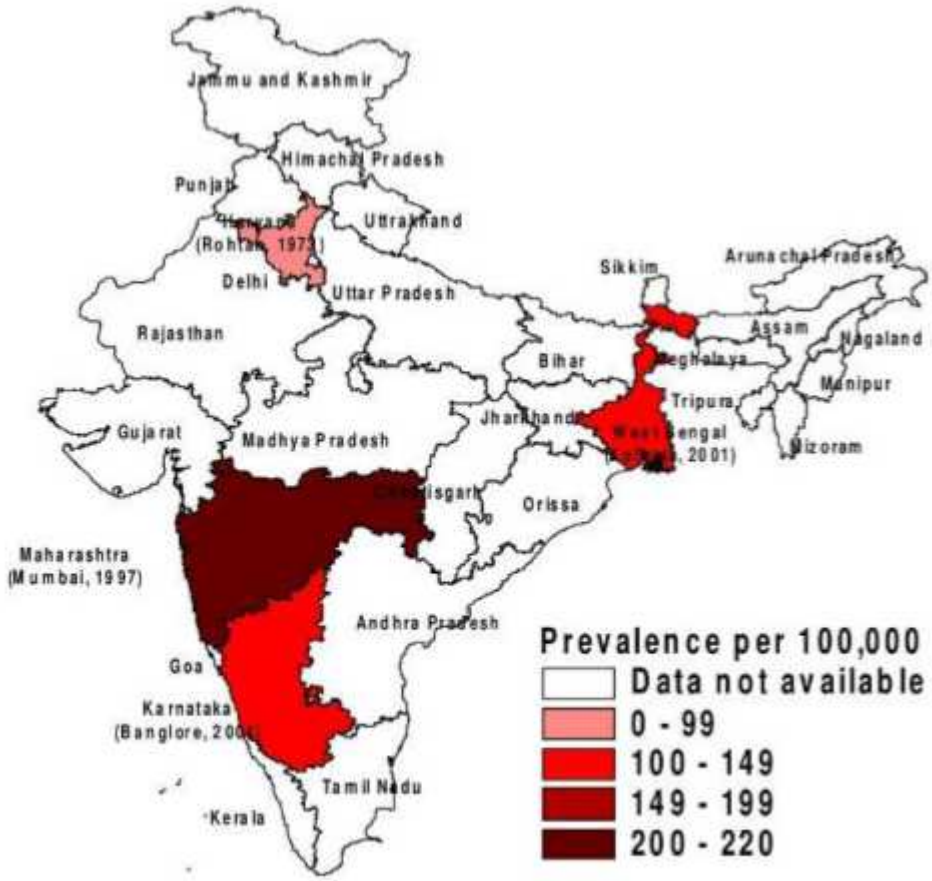
PREVALANCE RATE FOR STROKE IN INDIA (RURAL)

(1970-2004)



PREVALANCE RATE FOR STROKE IN INDIA (URBAN)

(1973-2004)



According to India stroke factsheet updated in 2012,

Prevelance of stroke - 84 to 262 per lakhs of population (rural),

334 to 424 per lakhs of population (urban).

Incidence of stroke - 119 to 145 per lakhs of population

Cases fatality rates - around 25% (urban), 37% (rural population) are died due to stroke and its complication in the first 28 days of stroke.

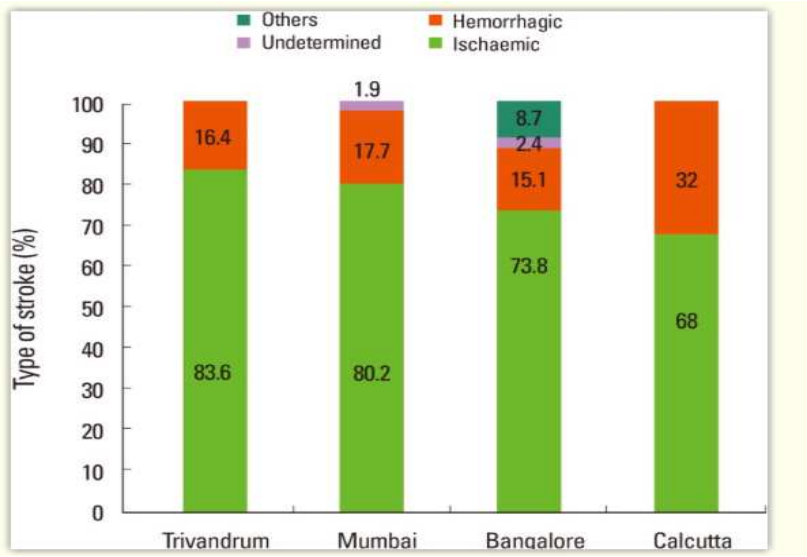
Mortality rate is highest in Kolkata studies (mortality rate –42%).

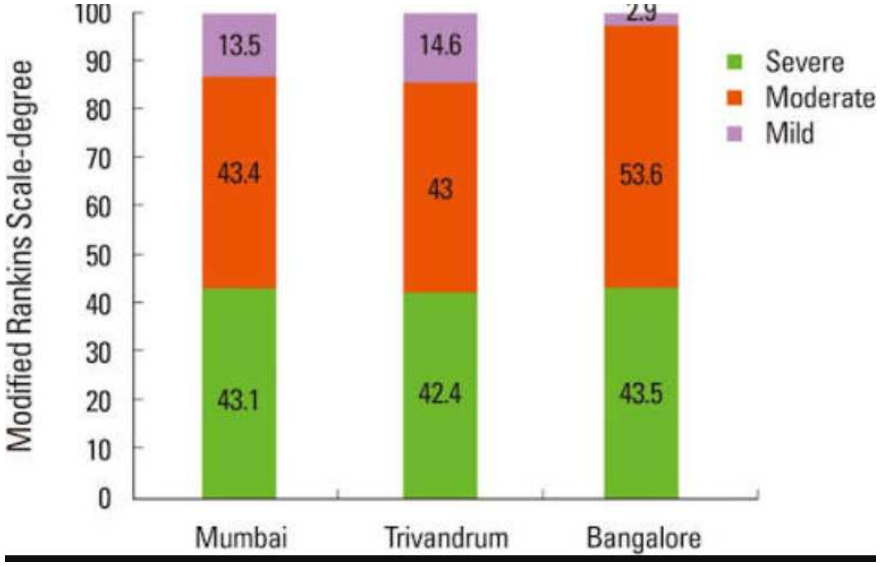
IV thrombolysis

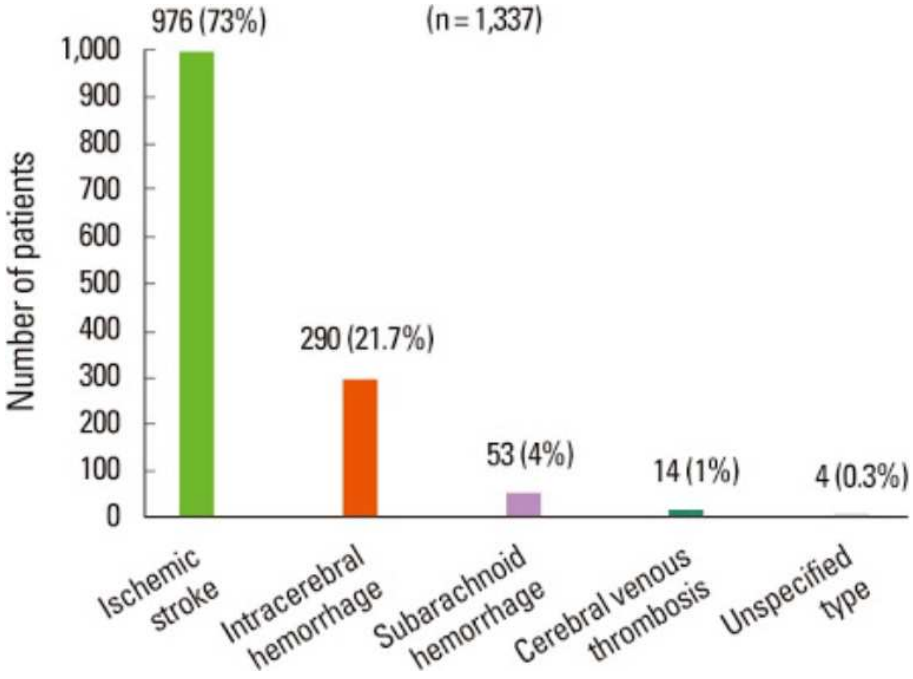
of stroke - 11% of the stroke.

Subtypes of Stroke - 68% cerebral infarct, 32% cerebral hemorrhage.[7]

SUBTYPES OF STROKE IN VARIOUS INCIDENCE STUDIES







Stroke ranks first among all neurological disease of adult life. Stroke presents with relatively sudden onset of neurological deficit. Stroke divided into two types – ischemic or hemorrhagic stroke. Ischemic stroke - as a result of occlusion of cerebral blood vessel which leads to cerebral ischemia and infarction.

Further classification of Ischemic stroke is based on underlying cause of vascular occlusion. Based on the cause, ischemic stroke, can arises from (1) large cerebral blood vessels atherosclerosis with superimposed thrombus, (2) small cerebral vessel occlusion in brain parenchyma, (3) cerebral embolism. Other causes includes arterial dissection, vasculitis, vasospasm, hyper-coagulable state, cortical vein thrombosis.

The other category consist of hemorrhage which may be intracerebral hemorrhage(ICH) or subarachnoid hemorrhage(SAH).The main causes of ICH are hypertension, coagulopathies, head trauma, vascular malformations, hemorrhagic transformation of ischemia. The most common cause of SAH is rupture of aneurysm of cerebral vessels of circle of willis. Other cause are head trauma, AV malformations.

Transient ischemic attack (TIA)- defined as temporary neurological deficit which recovers completely within 24 hours without any recidual deficit and with normal brain imaging.[8]

STROKE –RISK FACTORS

FIXED RISK FACTORS

A. Age - elderly are more at risk. After 55 years, risk doubles for every decade.[19]
B. Sex –male are at more risk than female except at extremes of age

C. Heriditary/Genetic factors

D. Race - Afro Carrribeans> Asians > Europeans

MODIFABLE RISK FACTORS

A. Hypertension - the most important risk factor.

B. Diabetes mellitus - it increases stroke incidence by 1.8 to 3.5 times. Hyperglycemia and insulin resistance are very important risk factors.[9]

C. Hyperlipidaemia

D. Cigarette smoking - risk doubling is seen in heaviest of smokers.[20]

E. Excessive alcohol intake

F. Obesity

G. Heart disease

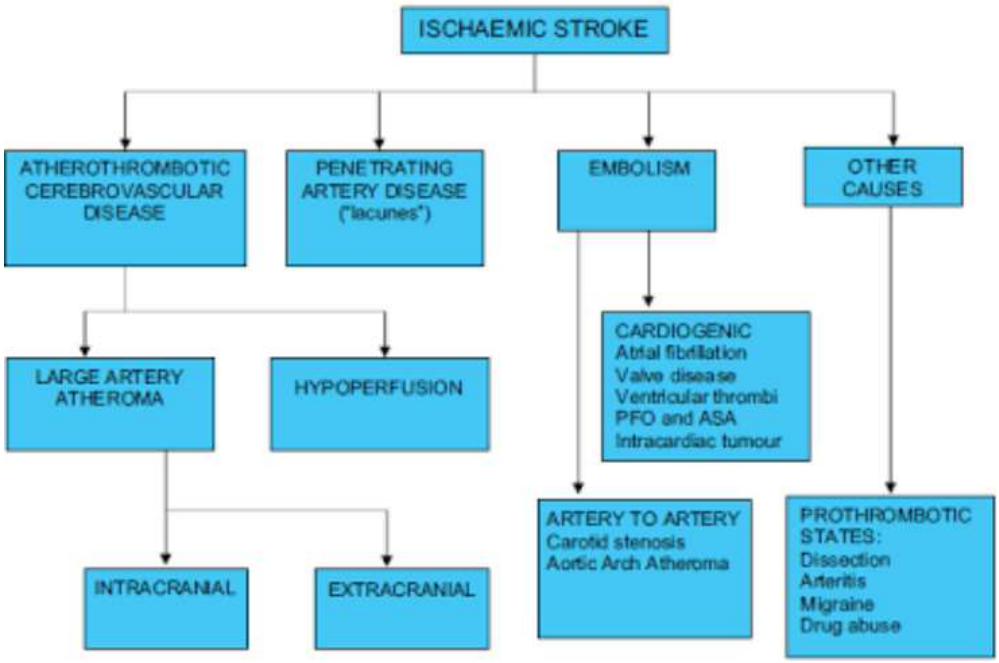
AF(Atrial fibrillation)

CCF(Congestive cardiac failure)

Infective endocarditis

H. Oestrogen containing drugs

(OCP, Hormone replacement therapy)



INCIDENCE OF RISK FACTORS IN VARIOUS TYPE OF STROKE (%)

	T	Lac	Emb	ICH	SAH
HSR					
Atherosclerosis*	56	37	34	11	5
Diabetes	26	28	13	15	2
Past hypertension	55	75	40	72	19
MRSR					
Angina pectoris	13	8	20	5	0
Past MI	23	16	40	12	0
Recent MI	7	12	12	3	0
Past hypertension	75	55	55	68	44

*Includes peripheral vascular disease, coronary artery disease, and neck bruits

HSR-Harvard stroke registry, MRSR-Michael Reese stroke registry, T-thrombosis, Lac-Lacune, Emb-embolism

WEIGHTING OF VARIOUS ECOLOGICAL FACTORS[1]

	T	Lac	Emb	ICH	SAH
Hypertension	++	+++		++	+
Severe hypertension		+		++++	++
Coronary disease	+++		++		
Claudication	+++		+		
Atrial fibrillation			++++		
Sick sinus syndrome			++		
Valvular heart disease			+++		
Diabetes	+++	+	+		
Bleeding diathesis				++++	+
Smoking	+++		+		+
Cancer	++		++		
Old age	+++	+	+	+	
Black or Asian ethnic origin	+	+		++	

CEREBROVASCULAR DISEASE AT DIFFERENT AGE[3]

1. Prenatal circulatory diseases leading to
   a. Porencephaly
   b. Hydranencephaly
   c. Hypoxic-ischemic damage
   d. Unilateral cerebral infarction
2. Perinatal and postnatal circulatory disorders resulting in
   a. Cardiorespiratory failure and generalized ischemia—*état marbre*
   b. Periventricular infarcts
   c. Matrix hemorrhages and ischemic foci in premature infants
   d. Hemorrhagic disease of the newborn
3. Infancy and childhood: vascular diseases associated with
   a. Ischemic infarction
   b. Congenital heart disease and paradoxical embolism
   c. Moyamoya disease
   d. Bacterial endocarditis, rheumatic fever, lupus erythematosus
   e. Sickle cell anemia
   f. Mitochondrial disorders (MELAS)
   g. Homocystinuria and Fabry's angiokeratosis
4. Adolescence and early adult life: vascular occlusion or hemorrhage with
   a. Pregnancy and puerperium
   b. Estrogen-related stroke
   c. Migraine
   d. Vascular malformations
   e. Premature atherosclerosis
   f. Arteritis
   g. Valvular heart disease
   h. Sickle cell anemia
   i. Antiphospholipid arteriopathy, plasma C protein deficiency and other coagulopathies
   j. Moyamoya, Takayasu diseases
   k. Arterial dissections
   l. Amyloid angiopathy
5. Middle age
   a. Atherosclerotic thrombosis and embolism
   b. Cardiogenic embolism
   c. Primary (hypertensive) cerebral hemorrhage
   d. Ruptured saccular aneurysm
   e. Arterial dissection
   f. Fibromuscular dysplasia
6. Late adult life
   a. Atherosclerotic thrombotic occlusive disease
   b. Embolic disease
   c. Lacunar stroke
   d. Brain hemorrhage (multiple causes)
   e. Multiinfarct dementia
   f. Binswanger disease

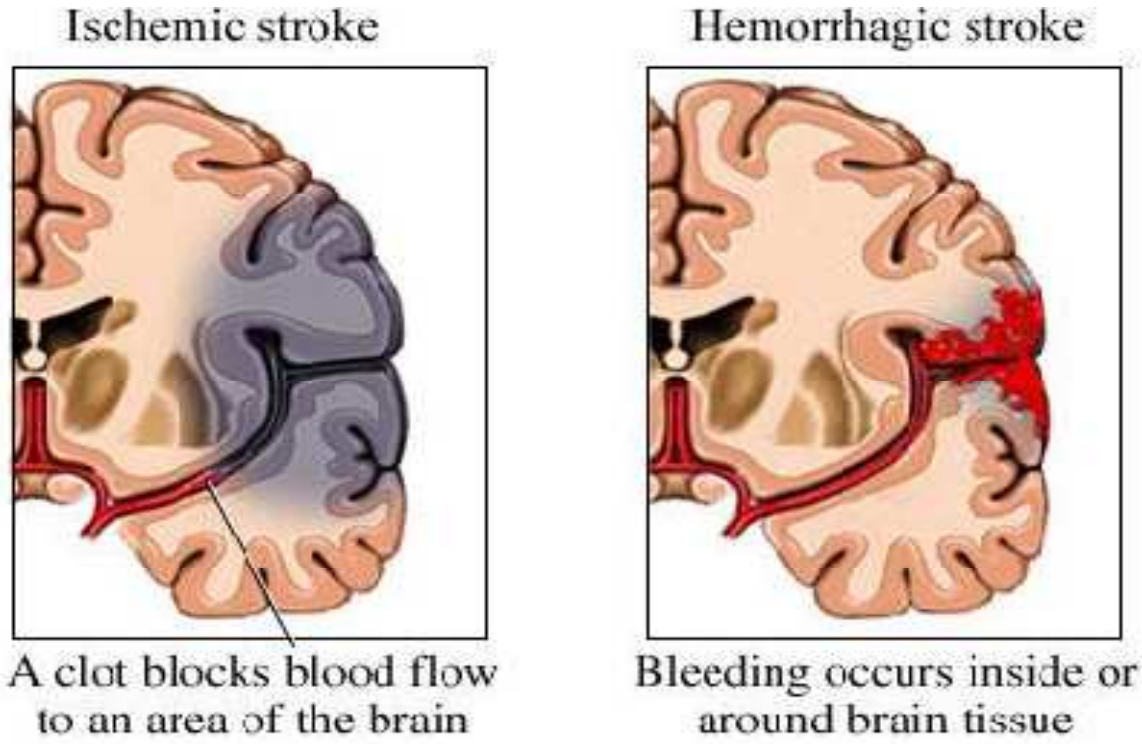
CLASSIFICATION OF STROKE

BASED ON PATHOGENESIS:

A) Ischemic stroke

B) Hemorrhagic stroke

C) Stroke of undetermined origin



A) ISCHEMIC STROKE

a) Thrombosis

Large vessels disease

lacunar stroke (small Vessels)

Dehydration

b) Embolic Occlusion

i. Cardio –embolic

a. Myocardial infarction (MI)

b. Mural thrombus

c . Atrial fibrillation (AF)

ii. Dilated cardiomyopathy (DCM)

c) Valvular lesions

i. Prosthetic valves

ii. Mitral stenosis

iii. Bacterial Endocarditis

iv. Atria septal aneurysm

v. Spontaneous ECHO contrast

vi. Paradoxical embolus:

Patent Foramen ovale, Atrial septal defect (ASD)

d) Artery to Artery

Aortic arch

Carotid artery bifurcation

Arterial dissection

e) Cardiogenic

i Marantic Endocarditis

ii. Libman sacks Endocarditis

iii. Intracardiac mass

iv. Mitral valve calcification

v. Atrial myxoma

f) Vasculitis

i. Primary CNS vasculitis

ii. Systemic Vasculitis –

1.Wegener'sGranulomatosis

2.Polyarteritis nodasa (PAN)

3.Takayasu arteritis

4. Giant cell arteritis

g) Meningitis

(TB, syphilis, bacterial, fungal, Bacterial, Zoster)

h) Hypercoagulable disorders

Antiphospholipid Antibody Syndrome

Protein C,S deficiency

Antithrombi III deficiency

Prothrombin v G20210 mutation

Systemic lupus erythematosis(SLE)

Thrombotic thrombocytopenic Purpura (TTP)

Disseminated Intravascular Coagulation (DIC)

Systemic Malignancy

Inflammatory bowel disease (IBD)

OralContraceptive pills(OCP)

Homocysteinemia.

Dysproteinemias

i) Eclampsia

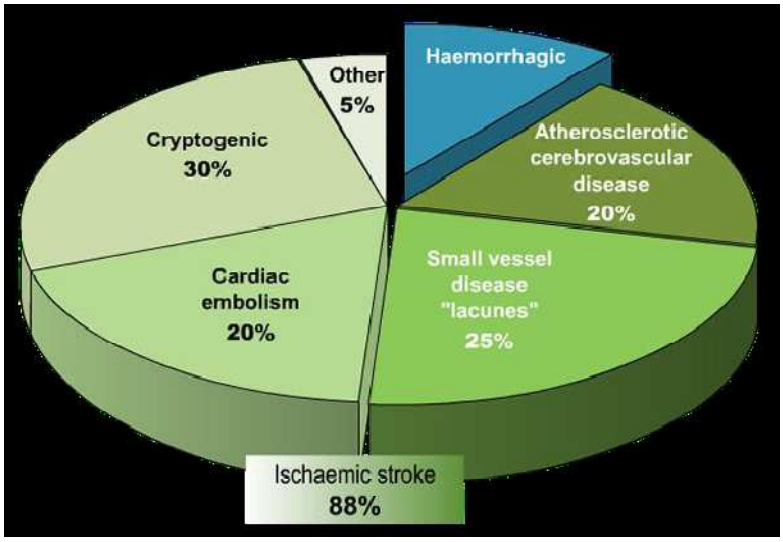
j) Drugs –cocaine, Amphetamine

B) HEMORRHAGIC STROKE

1. hypertension
2. rupture of cerebral aneurysm
3. head trauma
4. blood dyscrasias
5. drug induced (anticoagulation therapy or thrombolytic therapy)
6. bleeding in the brain tumors
7. miscellaneous cause

C) STROKE OF UNDETERMINED ORIGIN

1. leukariosis
2. aortic arch syndrome
3. Fibromuscular dysplasia
4. Binswanger's disease
5. moyamoya disease



CLINICAL CLASSIFICATION

(1) Based on arterial territory involved

(a) Anterior circulation stroke:

It may be

- Anterior cerebral artery (ACA) syndrome
- Middle cerebral artery (MCA) syndrome

(b) Posterior circulation stroke:

It may be

- Vertebro basilar artery syndrome
- Posterior cerebral artery syndrome

(2) Based on clinical manifestations:

(a) completed stroke:

It is rapid onset of stroke, with persistent neurological deficit but it does not progress beyond 96 hours.[3]

(b) Evolving stroke :

In this type, there is stuttering or gradual development of deficit

c) Reversible ischemic neurological deficit :

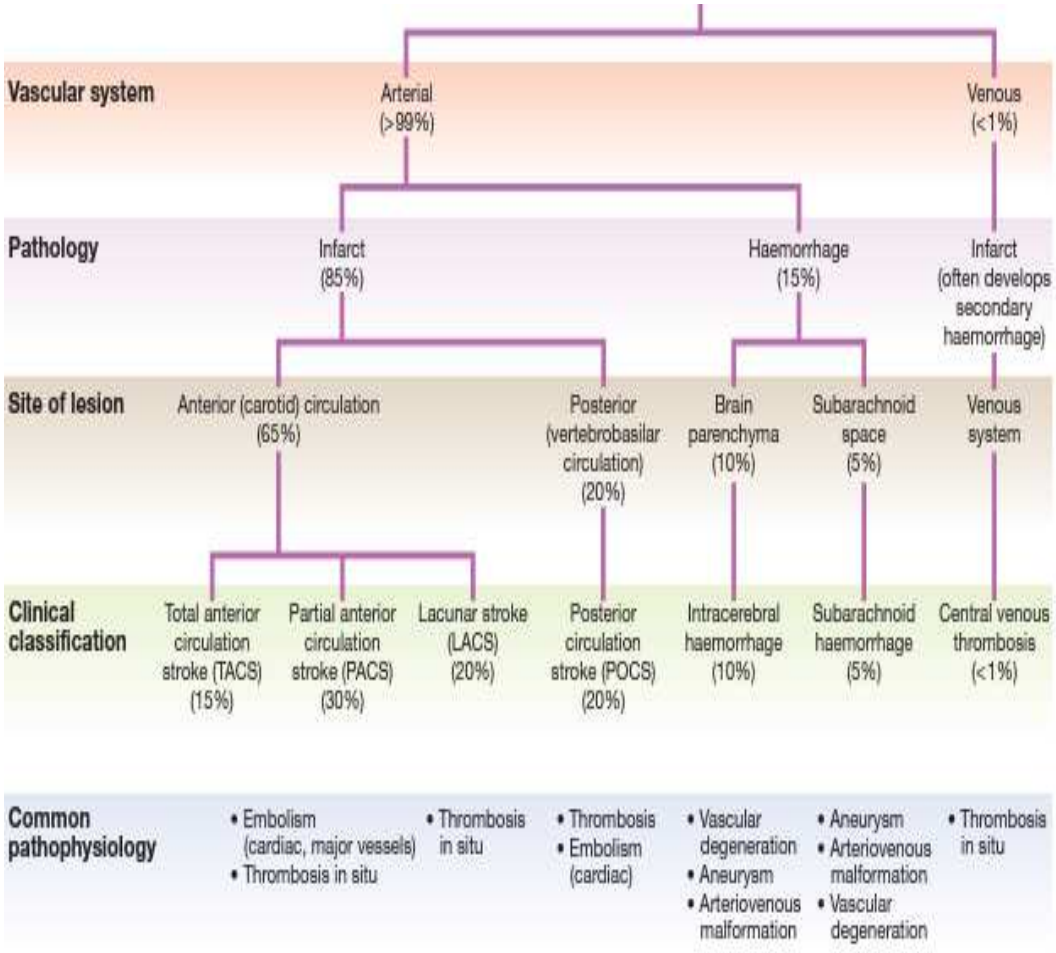
There will be neurological deficit but there will be

complete recovery within one week.

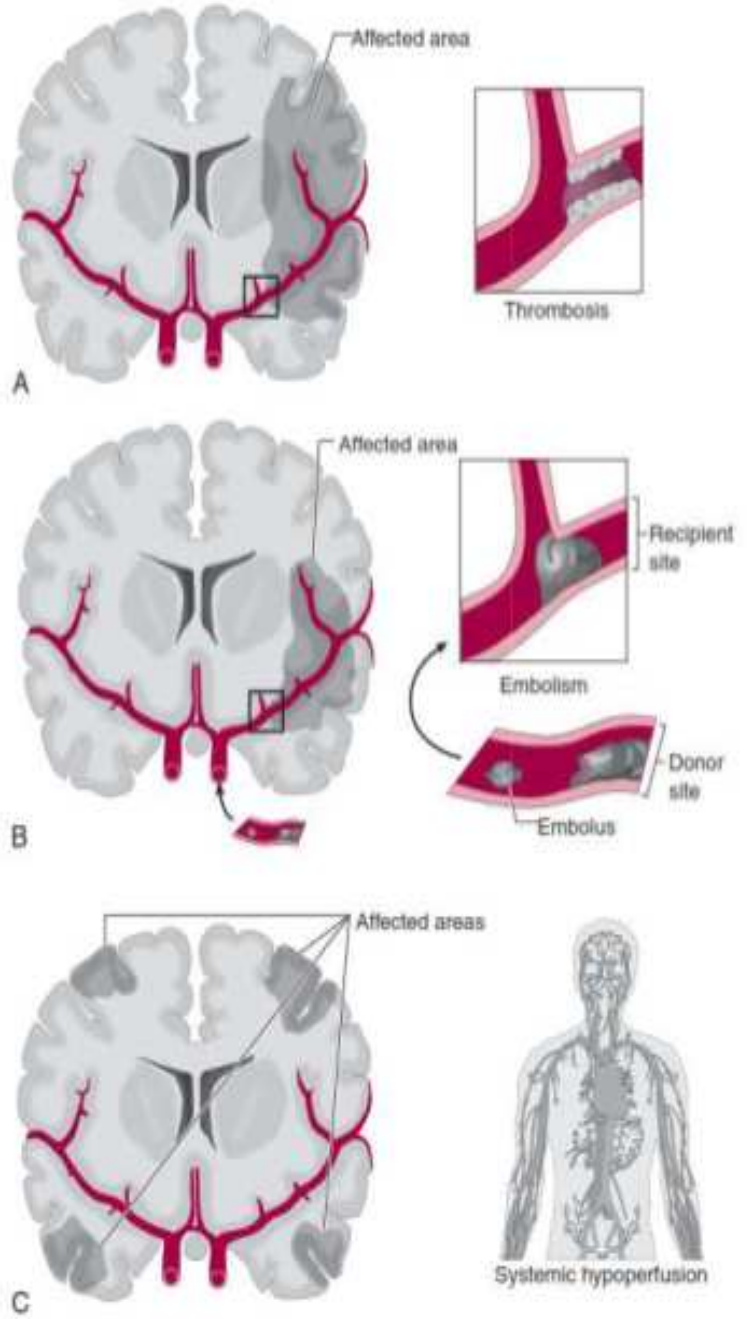
d) Transient ischemic attack (TIA):

TIA refers to focal neurological deficit which completely recovers within 24 hours.

STROKE



PATHOGENESIS OF DIFFERENT TYPES OF ISCHEMIC STROKE



Illustrations of the three major causes of brain ischemia. (**A**) Thrombosis. The *insert* shows a thrombus in an atherosclerotic artery leading to a brain infarct, (**B**) Embolism. A thrombus that originated in a donor source embolized to the recipient site (shown in the insert) causing an embolic brain infarct, and (**C**) systemic hypoperfusion. Infarcts are in border-zone regions.

PATHOPHYSIOLOGY OF STROKE

CEREBRAL AUTOREGULATION

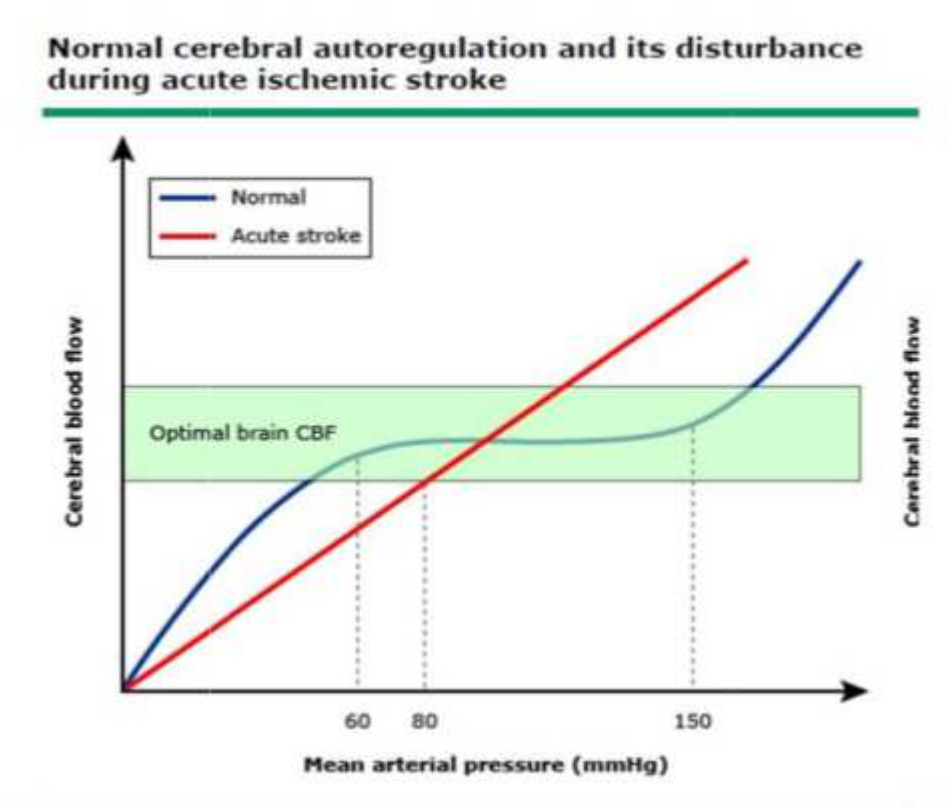
Cerebral blood flow normally depends on the amount of resistance of cerebral blood vessels, which depends on their circumference.[10] Cerebral blood vessels dilatation leads to increased amount of cerebral blood flow, while constriction has opposite effect. Cerebral blood flow was also determined by the cerebral perfusion pressure.

Cerebral autoregulation is the maintainence of constant blood flow inspite of changes in the perfusion pressure of brain. There are three mechanism which are thought to responsible for cerebral autoregulation. They are metabolic, myogenic, neurogenic.

Metabolic regulation is by the balance between the demand and oxygen supply through cerebral blood flow and it acts through vasoactive substance. It acts through negative feedback system.

Myogenic regulation –the transmural blood pressure are detected by smooth muscle in the arteriole and they are adjusted to keep constant blood flow.

Neurogenic regulation is by sympathetic innervations which controls the resistance in arterioles. Parasympathetic fibers which release nitric oxide also plays role.



Cerebral blood flow is maintained by cerebral autoregulation within a range of 60 to 150 mmHg of MAP (mean arterial Pressure). The limits may vary but beyond this range of mean arterial pressure, the brain will be unable to compensate for the perfusion pressure changes, and hence cerebral blood flow increases or decreases passively according to the corresponding changes in pressure, resulting in the risk of ischemia when there is low pressures and edema occurs at high pressures.

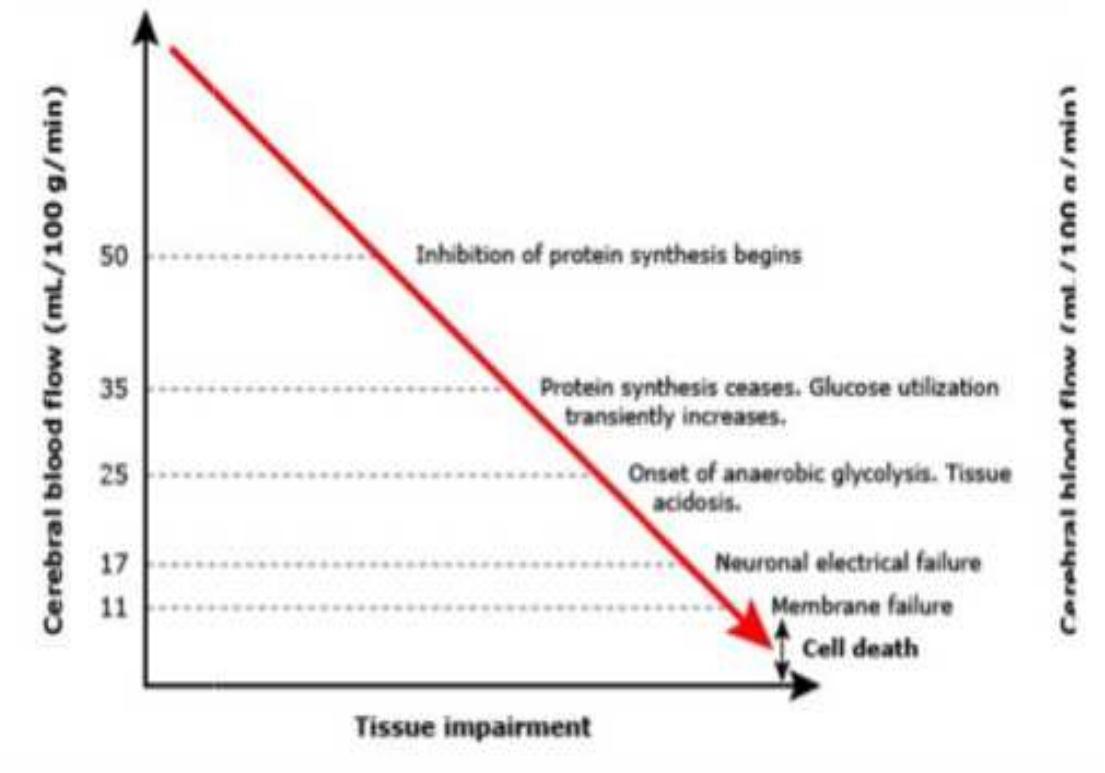
CEREBRAL AUTOREGULATION DURING STROKE

Cerebral auto regulation will get impaired in some diseases including ischemic stroke.[11,12] When perfusion pressure of brain decreased there will be compensatory cerebral vascular dilatation leading

to increased flow. When the autoregulation fails, when it falls below the compensatory ability of the brain then there will be decrease in the cerebral blood flow. Initially, there will be increase in the extraction fraction of the oxygen so that there will be maintenance in the level of oxygen supply to the brain. When there is continuous fall in the cerebral blood flow, other mechanisms come into play.

In hypertensive patient, cerebral auto regulation occurs at higher arterial pressures. So on suddenly reducing the blood pressure to normal levels in ischemic stroke would exacerbate the derangement of autoregulation which would lead to further decrease in cerebral blood flow.So it is safe to modestly decrease blood pressure in patient with acute ischemic stroke. There are no data on controlled trial to indicate decreasing blood pressure is beneficial in acute ischemic stroke. In patient with acute ischemic stroke, blood pressure should be decreased when there is malignant hypertension, concomitant myocardial ischemia, blood pressure >185/110mmhg and there is anticipation of thrombolytic therapy.

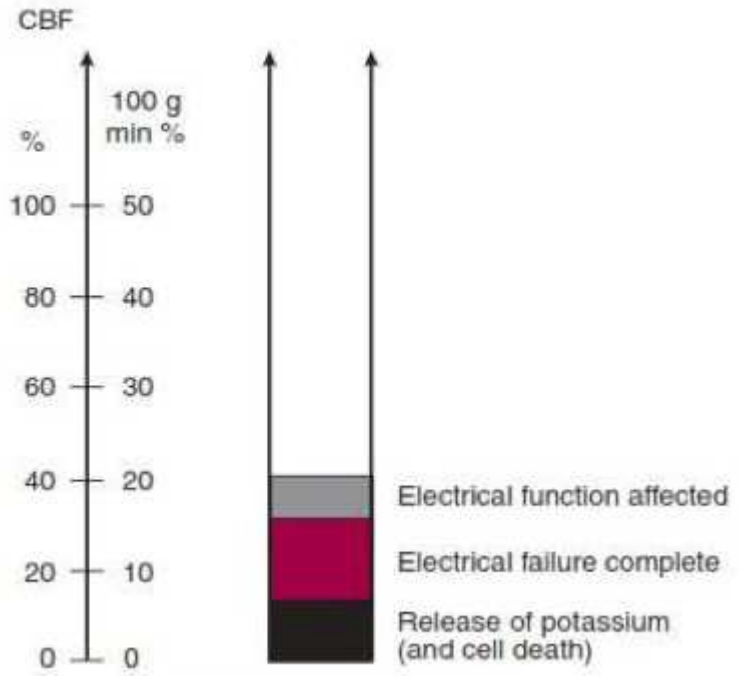
EFFECT OF DECREASED CEREBRAL BLOOD FLOW ON VITAL BRAIN FUNCTIONS



CONSEQUENCES OF REDUCTION IN BLOOD FLOW DURING STROKE

The human brain is more sensitive to ischemia even on short durations. Among the cardiac output, 20% is received by the brain.

The human brain has no own energy stores, so it completely depend on the blood flow for their delivery.Hence even brief deprivation in flow leads to death of the brain tissue affected. Reduction of cerebral blood flow results in a deprivation of oxygen and glucose during stroke.



Thresholds of brain ischemia.

In ischemic stroke .when the blood vessel is affected, the area which is supplied by the vessel, that is immediately surrounding the vessel get involved earlier. In this area if there is prolonged ischemia. then there will be death of the cells by necrosis. This area which underwent necrosis is known as cerebral infarct. The pheripheral area which receives blood flow-nutrients and oxygen through collaterals, will not die immediately and it can be revived by restoration of blood flow by timed intervention.[24]This area surrounding the dead cells is known as Ischemic penumbra.[1]

Factors Promoting Ischemia	Responses Limiting Ischemia
Decreased blood flow due to occlusion	Opening of collateral vascular channels
Embolization of clot	Passing and fragmentation of emboli
Activation of coagulation factors and inhibitors of thrombolysis	Activation of thrombolytic factors
Propagation of clot	Lysis of clot
Decreased blood flow due to hypotension, hypovolemia, low cardiac output	Improvement in general medical condition, especially after correction of abnormalities

The possible sequence of events in cerebral ischemia are

Depletion of ATP

Sodium, potassium, calcium ionic concentration changes

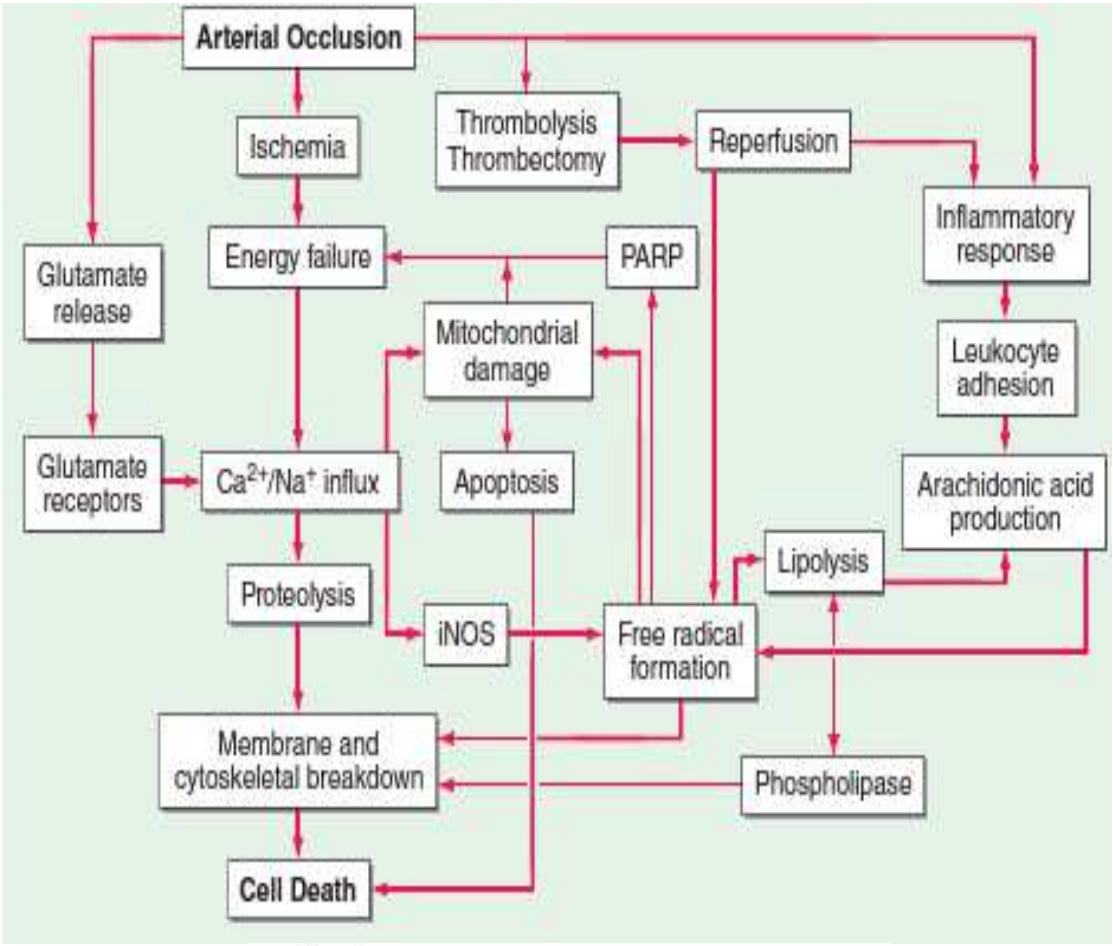
Acidosis due to increased amount of lactic acid

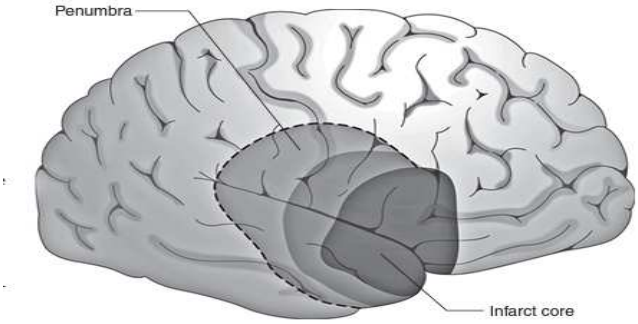
Oxygen free radicals

Proteolytic enzymes

Accumulation of water inside the cell

CASCADE OF CEREBRAL ISCHEMIA





CEREBRAL EDEMA

Cerebral edema in stroke can cause numerous secondary damages in brain-increasing intracranial pressure which leads to decreased cerebral blood flow and other is mass effect which causes herniation which may be life threatening.

In ischemic stroke two types of edema can occur.

1.cytotoxic edema

2.vasogenic edema

CYTOTOXIC EDEMA

Due to ischemia, there will be failure of energy dependent pumping system of sodium and calcium, which will lead to accumulation of water inside the cells resulting in cerebral edema[21,22,23] .Cytotoxic edema implies large volume of dying or dead cells implies poor outcome.

VASOGENIC EDEMA

The blood brain barrier breakdown occurs, resulting in leakage of osmotically active substance from intravascular to interstitial space which results in increased extracellular fluid volume.It does not necessarily implies neuronal injury and this extravascular fluid can be mobilized and removed.[1]

About 10% of ischemic stroke is massive because of this cerebral edema which may be severe to produce increased intracranial tension and herniation.

STROKE SYNDROMES BASED ON ARTERIAL TERITORRY INVOLEMENT

Artery involved	Syndrome	Pathophysiology
Anterior cerebral artery	Motor and/or sensory deficit (leg >> face, arm) Grasp, sucking reflexes Abulia, paratonic rigidity, gait apraxia	Embolic > atherothrombotic
Middle cerebral artery	Dominant hemisphere: aphasia, motor and sensory deficit (face, arm > leg > foot), may be complete hemiplegia if internal capsule involved, homonymous hemianopia Non-dominant hemisphere: neglect, anosognosia, motor and sensory deficit (face, arm > leg > foot), homonymous hemianopia	Embolic > atherothrombotic
Posterior cerebral artery	Homonymous hemianopia; alexia without agraphia (dominant hemisphere); visual hallucinations, visual perseverations (calcarine cortex); sensory loss, choreoathetosis, spontaneous pain (thalamus); III nerve palsy, paresis of vertical eye movement, motor deficit (cerebral peduncle, midbrain)	Embolic > atherothrombotic
Penetrating vessels	Pure motor hemiparesis (classic lacunar syndromes) Pure sensory deficit Pure sensory-motor deficit Hemiparesis, homolateral ataxia Dysarthria/clumsy hand	Small artery (lacunar) infarct
Vertebrobasilar	Cranial nerve palsies Crossed sensory deficits Diplopia, dizziness, nausea, vomiting, dysarthria, dysphagia, hiccup Limb and gait ataxia Motory deficit Coma Bilateral signs suggest basilar artery disease	Embolic = atherothrombotic
Internal carotid artery	Progressive or stuttering onset of MCA syndrome, occasionally ACA syndrome as well if insufficient collateral flow	Atherothrombotic > embolic

Anterior cerebral artery Infarct		
Relation to anterior communicating Artery	Distal (peripheral)	Proximal
1.	Contralateral hemiplegic Hemi sensory loss with predominant lower limb involvement	Complete hemiplegia
2.	No facial involvement	Facial involvement on the opposite side of the body with or without aphasia
3.	Urinary incontinence	
4.	Emotional disturbances	
5.	Presence of released reflexes	

Middle cerebral artery stroke		
Occlusion of Stem of Middle cerebral artery	Occlusion of proximal superior division of MCA	Occlusion of Inferior division of MCA.
a. Global aphasia	a. Motor weakness,	a.Wernicke's aphasia without weakness
b. Contralateralhemiplegia	B.Sensory disturbances.	B.Quadrantopsia sometimes.
c. Contralateral hemianaesthesia	c.Motor aphasia	c. ınon dominant hemisphere, hemi neglect and spatial agnosia can occur without weakness.
d. Contra lateral hemianopia		
e. Apractagnosia, dysarthria, contra lateral neglect in non dominant hemisphere involvement.		
The MCA supplies the upper extremity motor strip. So weakness of the arm and face is usually worse than that of the lower limb.		

Posterior cerebral artery syndrome	
Signs and symptoms	**Structures involved**
a.Homonymous hemianopia	Calcarine cortex
b.Cortical blindness, denial of blindness, apraxia of ocular movements	Bilateral occipital lobe involvement
c.Dyslexia without agraphia	Dominant calcarine lesions
d.Memory defect	Dominant temporal lobe

LACUNAR STROKE

Clinical features	Structure involved
Pure motor hemiparaesis	Infarct in the basis pontis, posterior limb of Internal capsule,
Pure sensory stroke	Ventral thalamus infarct
Ataxic hemiparaesis	Pons -Ventral portion infarct
Dysarthria and clumsy hand syndrome	Genu of internal capsule infarct

IMAGING STUDIES

CT SCAN

It helps in differentiation of infarct and hemorrhages. Infarct is seen as hypodense lesion whereas hemorrhage is seen as hyperdense area. Hypodense marking of involved vein, grey enhancement, post contrast enhancement of the involved vein suggest cortical venous thrombosis.

MERITS

- helps in differentiating infarct and hemorrhages and hence line of management can be decided.
- highly sensitive in detecting SAH.

DEMERITS

- In acute setting it may not detect infarct in the first 24 hours
- it may miss cortical surface small infarct.
- not detect lesion in posterior fossa due to artifact.

MRI SCAN

- It is more sensitive for early brain infarction.
- it is considered superior to ct scan for detecting posterior fossa and cortical infarction.
- MR Angiogram helps in detecting stenosis of intracranial vessels

FINDINGS OF CT IN CEREBRAL INFARCTION [25]

Timing of Infarct	CT Findings
a.Hyperacute (<12 hours)	Lentiform Nucleus obscuration Increased dense lesions (25 – 50 %) Normal (50%)
b.Acute (12 to 24 hours)	Effacement of sulcus,loss of grey and white matter differentiation (Insular ribbon sign)
c.Days 1day to 7 days	Transformation of infarct into hemorrhages, Enhancement of Gyrus, Mass effect, Low density areas which is wedgeshaped, involving white and greymatter.
d.Weeks :1-8	Resolving of mass effects, persistence of contrast enhancement.
e.Months to years	Encephalomalacia changes. Loss of Volume

FINDINGS OF MRI IN CEREBRAL INFARCTION

Stage of Infarction	*MRI findings*
Immediate	Intravascular contrast enhancement; Alteration of perfusion/diffusion coefficient
< 12 hours	Anatomic changes of T_1 images (gyral thickening, sulcal effacement loss of grey-white interface)
12 to 24 hours	Hyperintensity, mass effect, leptomeningeal enhancement
1 to 3 days	Obvious abnormality in T_1 and T_2 images (early parenchymal contrast enhancement, haemorrhagic transformation)
4 to 7 days	Parenchymal enhancement, Haemorrhage (in 25%)
1 to 8 weeks	Mass effect resolves, decreased signal on T_2 images, enhancement persists, haemorrhage signal evolves
Months to years	Encephalomalacic changes, volume loss in affected area, haemosiderin staining (in significant haemorrhage)

TREATMENT OF ACUTE ISCHEMIC STROKE

MEDICAL SUPPORT

Blood pressure should be lowered [13]

- when BP >185/110mmHg,thrombolytic therapy anticipated.
- malignant hypertension
- concomitant myocardial ischemia

Serum glucose should be maintained and kept below180mg/dl, if needed by insulin infusion.[13]

Fever will be detrimental, should be lowered by surface cooling and antipyretics.[14]

For cerebral edema, iv mannitol, water restriction can be tried. But hypovolemia should be avoided.

INTRAVENOUS THROMBOLYSIS

INDICATIONS [13]

Clinical diagnosis of stroke

Time between symptoms and drug administration<=4.5hrs

Age >=18yrs

No hemorrhage in CT and edema <1/3 of MCA Territory

IV THROMBOLYSIS [3]

Inclusion criteria

- Acute ischemic stroke with measurable neurologic deficit
- Onset of symptoms less than 3 h before institution of treatment (all preliminary diagnostic tests must be completed)
- Onset of symptoms between 3 and 4.5 h and patient younger than 80 years, and with NIH stroke score below 25, nondiabetic, and having received no recent anticoagulant medication, regardless of INR*
- Age over 18 years

Exclusion criteria

- Cerebral imaging showing intracerebral hemorrhage
- Cerebral imaging demonstrating large infarction, >1/3 territory of a cerebral hemisphere (CT hypodensity or diffusion restriction on MRI)
- Head trauma within 3 months prior to stroke
- History of intracranial hemorrhage
- Elevated blood pressure; systolic >185 mm Hg or diastolic >110 mm Hg that has not responded to medications
- Active bleeding or arterial puncture at noncompressible site
- Hematologic alternations including
  - Platelet count <100,000/mm³
  - Heparin administered within 48 h resulting in a PTT above normal range
  - Current use of anticoagulation with INR >1.7 or prothrombin time >15 s
- Blood glucose <50 mg/dL (2.7 mmol/L)

Relative contraindications

- Minor or resolving stroke
- Seizure at onset
- Major surgery or trauma within 14 days
- Gastrointestinal or urinary bleeding within 21 days
- Myocardial infarction within 3 months

ANTITHROMBOTIC TREATMENT

PLATLET INHIBITION

Aspirin is the only agent which was effectively proven for acute ischemic stroke.[17]Clopidogrel is under trial for preventing stroke following TIA.It can be given to patients who show resistance to aspirin.[18]

ANTICOAGULATION

Anticoagulation has no benefit for atherothrombotic stroke and also it increases risk of hemorrhage.[16]It is useful in cortical venous thrombosis and in patient with atrial fibrillation.

ENDOVASCULAR TECHNIQUE

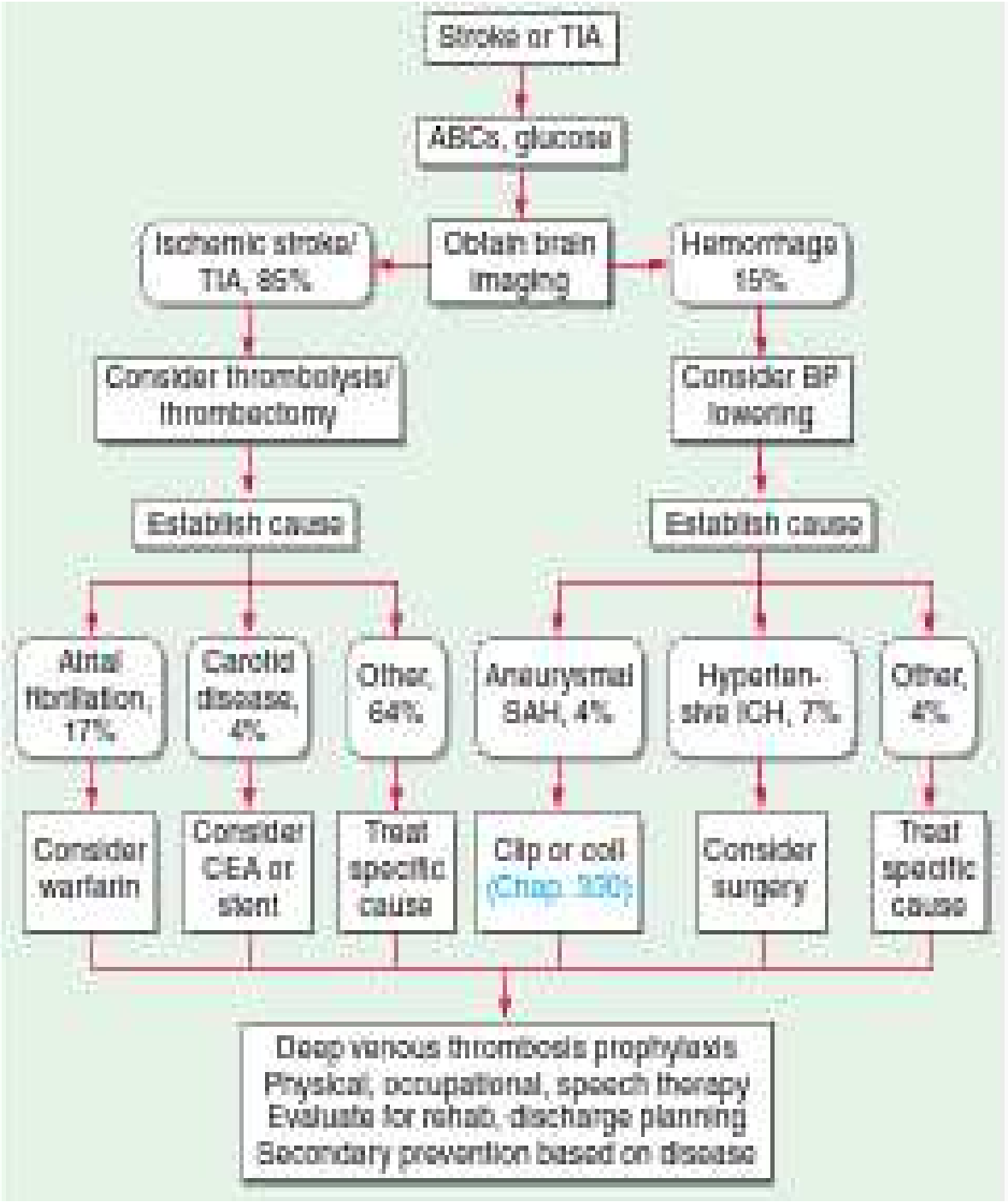
NEUROPROTECTION

STROKE CENTRES AND REHABILITATION

- Physical,occupational,speech therapy

Nutritional maintenance (especially if dysphagia is present)	Balanced diet that conforms to suggested calories and content (e.g., low cholesterol and low salt), vitamins when indicated, intravenous feeding, nasogastric tubes, gastronomy
Pulmonary complications (aspiration, pneumonia atelectasis, pulmonary emboli)	Care or avoidance in oral feeding; in dysphagics, study of swallowing before oral feeding; respiratory therapy; early antibiotic treatment of infection; no smoking; anticoagulants (miniheparin or heparinoids); use of special leg boots to prevent phlebothrombosis
Immobility (body or one or more limbs)	Frequent full range-of-motion exercises, frequent turning, prevention of pressure palsies and joint dislocations by slings, and careful limb positioning
Urinary-tract complications (bladder distension, urinary retention, infection)	Catheterization using sterile technique when needed; avoidance when possible of indwelling catheters; early antibiotic treatment; urinary acidification
Skin (decubiti)	Careful, frequent turning; pillows and pads to protect pressure areas; water beds; skin surveillance
Psychological (apathy and depression)	Positive outlook; entire medical care personnel functioning as a team; antidepressants

ALGORITHM FOR STROKE MANAGEMENT[13]



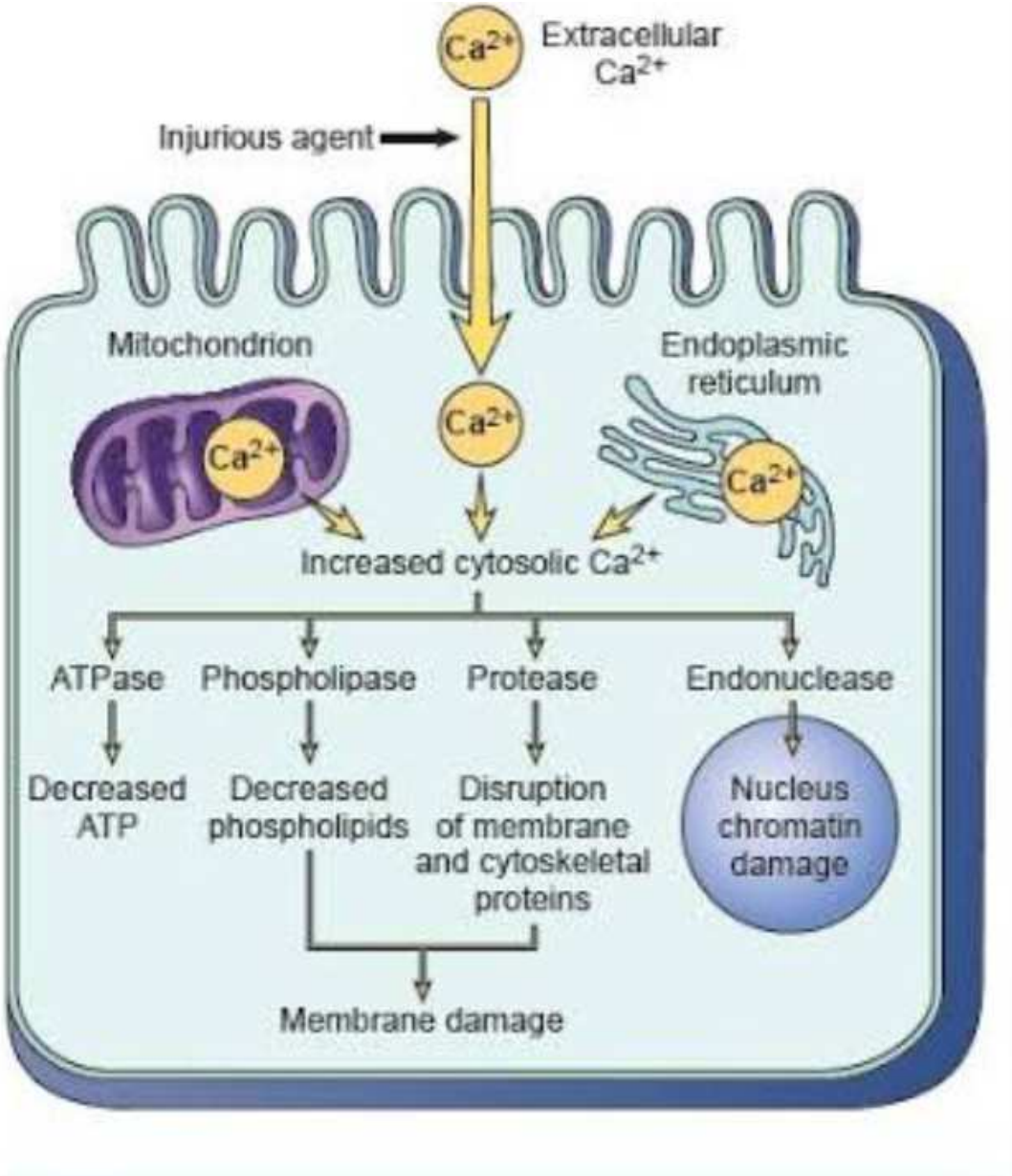
ROLE OF CALCIUM IN ISCHEMIC STROKE

Calcium ions play a important physiological role in the pathophysiology of cerebral ischemia. It has been studied with its relationship with stroke incidence and risk factors of stroke. It has been demonstrated that in cerebral ischemia, there is decrease in calcium. It has also been demonstrated that disturbed calcium homeostasis and to events such as proteolysis and lipolysis which are calcium triggered events are related to gross brain damage, involving edema and infarction.[27]

Cell calcium (ca2+) metabolism which occurs during and immediately after a transient period of ischemia influences the sequence of events that leads to subsequent progressive neuronal injury. For instance, ischemia and hypoxia, causes rapid translocation of calcium($Ca^{2+)}$ from extracellular spaces to intracellular spaces of brain tissues . This intracellular Ca accumulation leads to various neuronal damage by triggering the multiple cycle of cytotoxic events.

A coupling exists between the influx of calcium into cells and the subsequent production of reactive oxygen species-free radicals. Mitochondrial accumulation of calcium and oxidative stress can trigger the opening of a high-conductance pore which is present in the inner mitochondrial membrane.[29] This mitochondrial permeability transition (MPT) pore leads to a collapse of the electrochemical potential for

hydrogen ions(H+), thereby leads to arrest of ATP production and it triggers the production of reactive oxygen species.[29]



Calcium plays a important role in the physiology, biochemistry of cell. It also plays an vital role in signal transduction pathways and it acts as a second messenger. Numerous enzymes require calcium ions as a cofactor as that of blood-clotting cascade[26] . Extracellular calcium is very

important for proper maintenance of the potential difference across the excitable cell membranes.

Many studies has been done and found that higher level of serum calcium levels at the time of admission are associated with smaller cerebral infarct volumes in patients affected with acute ischemic stroke.[28]

SERUM ALBUMIN IN ACUTE ISCHEMIC STROKE

Human serum albumin acts as a unique multifunctional protein with marked neuroprotective properties.[30] Albumin has numerous intravascular effects. It reduces hematocrit level, influences aggregation of erythrocyte by increasing low shear viscosity, decreasing sedimentation of erythrocyte under no flow conditions.

Albumin acts as a major antioxidant defense against oxidizing agents. The neuroprotective property of human albumin in ischemic stroke also resides in its effect of antagonism of stagnation, thrombosis, adhesion of leucocyte within postcapillary microcirculation .

Many experimental animal studies has been done and it showed that human albumin therapy in acute stroke improves neurological function and markedly reduces the volume of cerebral infarction, decreases brain swelling in animals[31]. Many human studies has been done and it showed that high serum albumin level is associated with decreased poor outcome in acute ischemic stroke.[32]

NATIONAL INSTITUTE OF HEALTH STROKE SCALE (NIHSS)

NIHSS was developed to assess the severity of stroke.It comprises totally of 11 items. Maximum possible score 42.

SCORE	STROKE SEVERITY
0	NO STROKE SYMPTOMS
1-4	MINOR STROKE
5-15	MODERATE STROKE
16-20	MODERATE-SEVERE STROKE
21-42	SEVERE STROKE

NIHSS

Tested Item	Title	Response & Scores
1A	Level of Consciousness	0 – Patient is very alert 1 – Ready to fall asleep, lack of attention, patient will respond to painful stimuli 2 – Patient is not alert or oriented to time, person, place and remains in a state of confusion or frank delirium 3 – Patient is Comatose and not responding to painful stimuli
1B	Orientation Questions	0 – Here patient answers correctly to 2 simple questions. 1 – Patient will answer 1 question correctly 2 – Patient will not answer correctly to any question.
1C	Response to Commands	0 – Patient will do both work and tasks perfectly 1 – Patient will do one task perfectly 2 – Patient will not do both tasks

2	Gaze	0 – Patient has normal horizontal movements 1 – Patient can have gaze palsy which is partial 2–Complete ophthalmoplegia
3	Field of vision	0 – Patients visual field is normal 1 – Patient will have Hemi-anopia which is partial 2 – Patient will have Hemi-anopia which is complete 3 – Here Hemi-anopia is bilateralation
4	Facial Movements	0 – Normal 1 – Here facial palsy is subtle 2 – Patient will have facial weakness which is incomplete 3 – Here facial palsy is complete which is unilateral

5	Motor Functions (Arm) a) Left b) Right	0 – No fall when both forearms are stretched out and kept in supinated position for 10 sec 1 – Fall of forearm and hand occurs but does not hit the bed 2 – Forearm and hands fall and hits the bed 3 – No movement against gravity 4 – Total paralysis
6	Motor Functions (leg) a) Left b) Right	0 – No fall of leg for 5sec 1 – Fall of leg occurs but it doesn't hit the bed. 2 – Fall of leg occurs and hits the bed. 3 – No movement against gravity 4 – Total paralysis
7	Limb Inco-ordination	0 – Normal 1 – Inco-ordination of only one limb 2 – Inco-ordination of two limbs

8	Sensory	0 – Patient will not have any sensory loss 1 – Here sensory loss is mild 2 – Here patient will have severe sensory loss
9	Language	0 – Patient can communicate and comprehend the language properly
10	Articulation	0 – Normal 1 – Articulation defect is mild 2 – Articulation defect is severe
11	Extinction or inattention (Neglect)	0 – Normal 1 – One modality of sensation is loss 2 – Severe loss of sensation

MODIFIED RANKIN SCALE (MRS)

TOTAL SCORE 0-6

Score	Observations
0	Patient should not have any symptoms at all
1	Patient should not have any significant disability in spite of presence of symptoms and can able to perform routine daily normal activities
2	Patient will have slight disability and the person cannot perform all routine activities but manages to do his personal work without help
3	Patient is having moderate disability and needs some help, but able to walk without assistance.
4	Patient will have moderately severe disability and cannot walk without help and unable to do his personal affairs without assistance
5	Here patient is having severe disability and the affected individual is bedridden, urinary incontinence will be present and needs continuous nursing care and attention
6	Dead

MATERIALS AND METHODS

MATERIALS AND METHODS

SETTING

This study was conducted at the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital (RGGGH), Madras Medical College, Chennai.

ETHICAL COMMITTEE APPROVAL

Obtained

STUDY DURATION

This study was conducted over a period of six months.

STUDY POPULATION

Patients who are admitted with Acute ischemic stroke to the medical wards at the Institute of Internal Medicine.

SAMPLE SIZE

70 Patients

TYPE OF STUDY

Observational study

INCLUSION CRITERIA

Patients

Age 18-60 yrs

Those with Acute ischemic stroke within 48 hrs of presentation.

EXCLUSION CRITERIA

Age > 60 yrs

Hemorrhagic stroke

Those presenting with ischemic stroke after 48 hrs of onset

Chronic renal failure

Hepatic failure

Recent myocardial infarction

Congestive cardiac failure

Cardiac arrhythmia

Fever/recent infection

Uncontrolled DM

Recurrent CVA

Those on calcium supplementation or on drugs affecting serum calcium.

Malignancy

DATA COLLECTION AND METHODS

On patients who have been admitted in medicine ward, RGGGH, Chennai, an observational study on acute ischemic stroke patients for period of 6 months. Patients selected for clinical study as per inclusion and exclusion criteria. Detailed history taking and clinical examination will be done. Serum levels of calcium and albumin will be estimated.

Severity of stroke will be assessed using National Institute of Health Stroke Scale(NIHSS) and one week functional outcome was assessed using modified rankin scale(mRS).

Patients were classified in to four quartiles based on corrected serum calcium as C1, C2, C3, C4 and based on serum albumin as A1, A2, A3, A4.

CALCIUM QUARTILES	CORRECTED CALCIUM
C1	<=8.59 mg/dl
C2	8.60-8.99 mg/dl
C3	9.0-9.39 mg/dl
C4	>9.40 mg/dl

ALBUMIN QUARTILES	SERUM ALBUMIN
A1	< 3.49 mg/dl
A2	3.50-3.99 mg/dl
A3	4.00-4.49 mg/dl
A4	>4.5 mg/dl

NIHSS -Totally 11 items, maximum possibility score 42

MODIFIED RANKIN SCALE- 0-6

Corrected Serum calcium and serum albumin were correlated with severity and outcome of acute ischemic stroke by NIHSS and mRS scale.

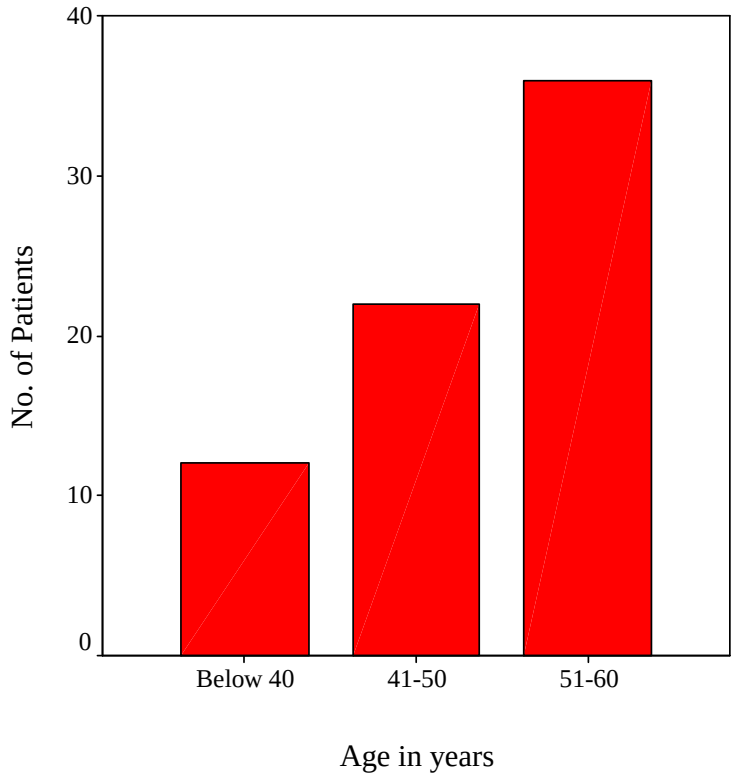
All the data obtained were entered in the proforma(enclosed).

Data were analyzed using SPSS package and by chi-square tests, ANOVA.

OBSERVATIONS AND RESULTS

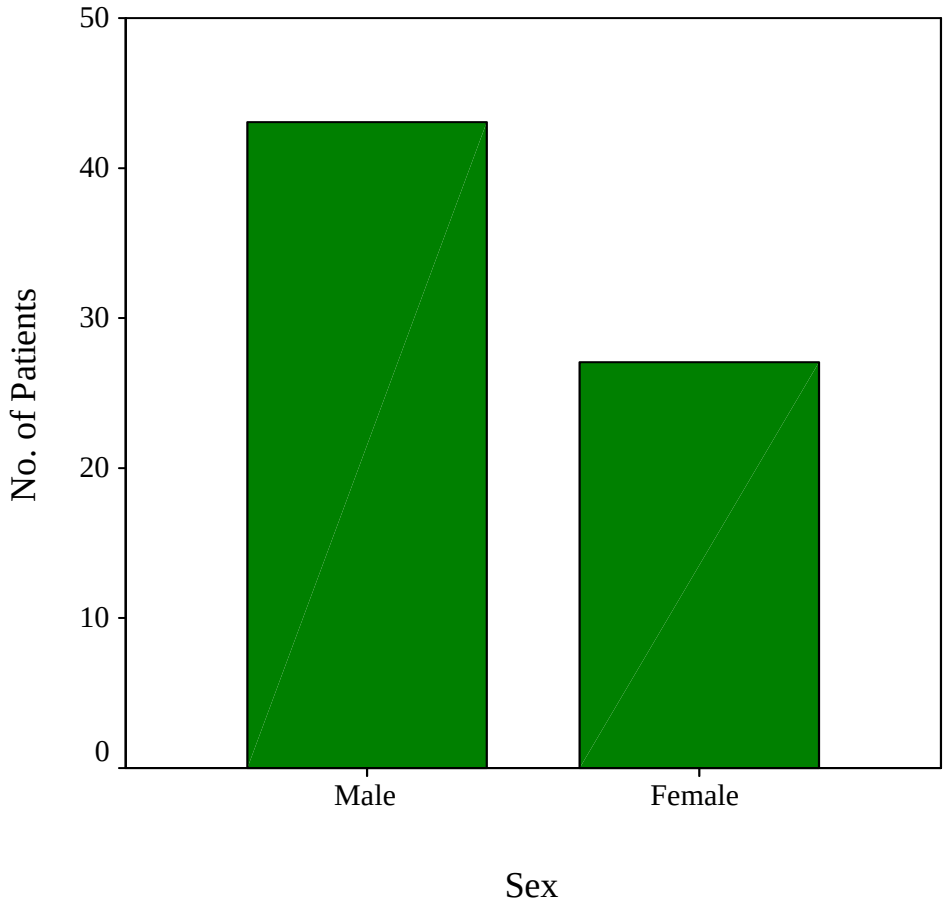
AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	Percent
Below 40	12	17.1
41-50	22	31.4
51-60	36	51.4
Total	70	100.0



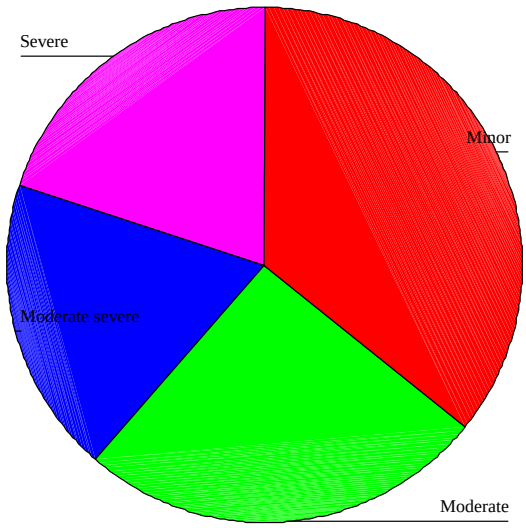
SEX DISTRIBUTION

SEX	NO OF PATIENTS	Percent
Male	43	61.4
Female	27	38.6
Total	70	100.0



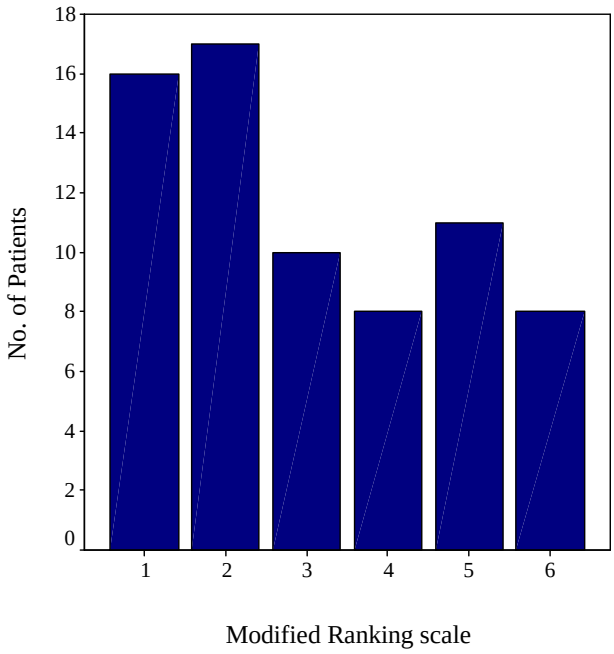
NIHSS SCORE AMONG THE STUDY GROUP

NIHSS	NO OF PATIENTS	Percent
Minor (0-4)	25	35.7
Moderate (5-15)	18	25.7
Moderate severe (16-20)	13	18.6
Severe (21-42)	14	20.0
Total	70	100.0



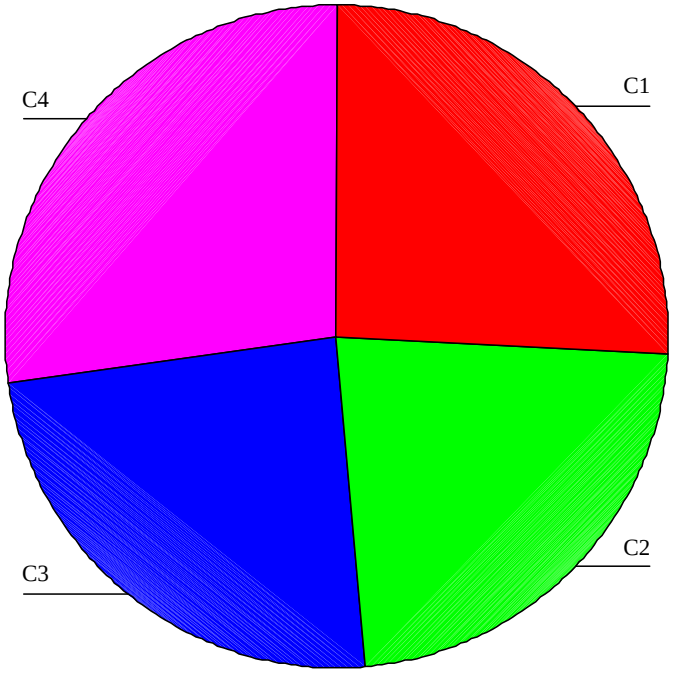
MODIFIED RANKIN SCALE AMONG STUDY GROUP

mRS	NO OF PATIENTS	Percent
1	16	22.9
2	17	24.3
3	10	14.3
4	8	11.4
5	11	15.7
6	8	11.4
Total	**70**	**100.0**



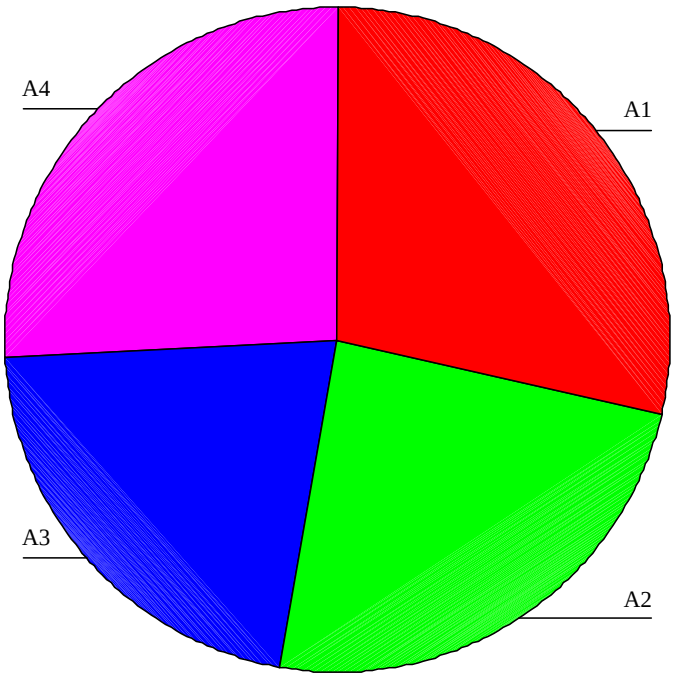
DISTRIBUTION OF PATIENTS IN VARIOUS CALCIUM QUARTILES

QUARTILES	CORRECTED CALCIUM (in mg/dl)	NO OF PATIENTS	Percent
C1	<=8.59	18	25.7
C2	8.60-8.99	16	22.9
C3	9.0-9.39	17	24.3
C4	>=9.40	19	27.1
Total		**70**	**100.0**



DISTRIBUTION OF PATIENTS IN VARIOUS ALBUMIN QUARTILES

ALBUMIN QUARTILES	SERUM ALBUMIN (in mg/dl)	NO OF PATIENTS	Percent
A1	<=3.49	20	28.6
A2	3.50-3.99	17	24.3
A3	4.00-4.49	15	21.4
A4	>=4.5	18	25.7
Total		70	100.0



HYPERTENSION AMONG STUDY POPULATION

HYPERTENSION	NO OF PATIENTS	Percent
Yes	44	62.9
No	26	37.1
Total	70	100.0

DIABETES MELLITUS AMONG STUDY POPULATION

DIABETES MELLITUS	NO OF PATIENTS	Percent
Yes	31	44.3
No	39	55.7
Total	70	100.0

MEAN AGE DISTRIBUTION IN DIFFERENT CALCIUM QUARTILES

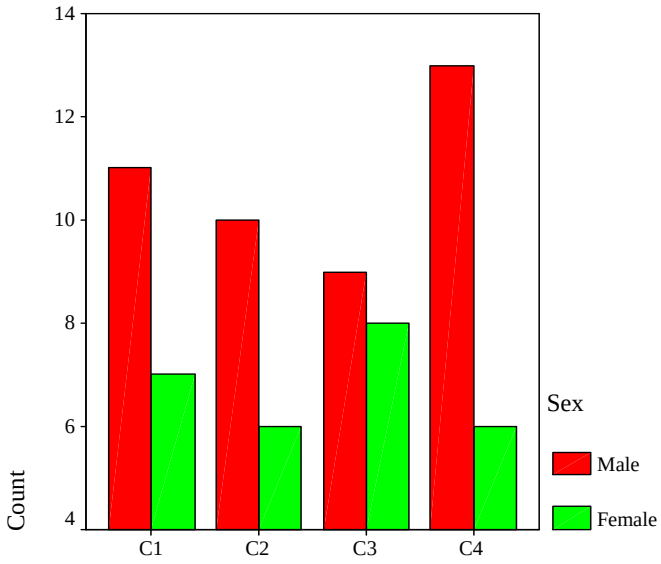
S.NO	CALCIUM QUARTILES	NO OF PATIENTS	MEAN AGE (YEARS)	
1	C1	18	49.06	
2	C2	16	49.63	p value
3	C3	17	48.59	0.966
4	C4	19	48.21	Not
	Total	70	48.84	significant

MEAN AGE DISTRIBUTION IN DIFFERENT ALBUMIN QUARTILES

S.NO	ALBUMIN QUARTILES	NO OF PATIENTS	MEAN AGE (YEARS)	
1	A1	20	49.30	p value
2	A2	17	48.65	0.955
3	A3	15	49.47	Not
4	A4	18	48.00	significant
	Total	70	48.84	

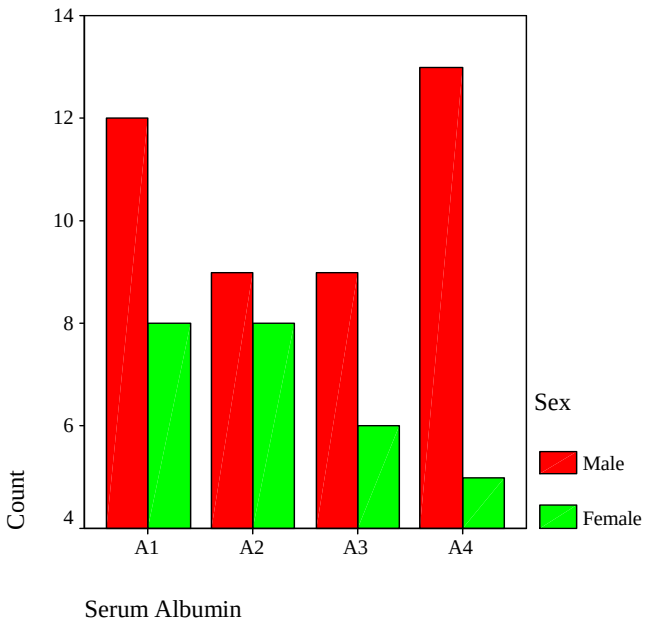
MEAN SEX DISTRIBUTION IN DIFFERENT CALCIUM QUARTILES

			Sex		Total	
			Male	Female		
Corrected Serum Calcium	C1	NO OF PATIENTS	11	7	18	P value 0.821 Not significant
		% within Sex	25.6%	25.9%	25.7%	
	C2	NO OF PATIENTS	10	6	16	
		% within Sex	23.3%	22.2%	22.9%	
	C3	NO OF PATIENTS	9	8	17	
		% within Sex	20.9%	29.6%	24.3%	
	C4	NO OF PATIENTS	13	6	19	
		% within Sex	30.2%	22.2%	27.1%	
Total		NO OF PATIENTS	43	27	70	



MEAN SEX DISTRIBUTION IN DIFFERENT ALBUMIN QUARTILES

			Sex		Total	
			Male	Female		
Serum Albumin	A1	NO OF PATIENTS	12	8	20	P value 0.698 Not significant
		% within Sex	27.9%	29.6%	28.6%	
	A2	NO OF PATIENTS	9	8	17	
		% within Sex	20.9%	29.6%	24.3%	
	A3	NO OF PATIENTS	9	6	15	
		% within Sex	20.9%	22.2%	21.4%	
	A4	NO OF PATIENTS	13	5	18	
		% within Sex	30.2%	18.5%	25.7%	
Total		Count	43	27	70	



PATIENTS WITH HYPERTENSION IN DIFFERENT CALCIUM QUARTILES

			Hypertension		Total	
			Yes	No		
Corrected Serum Calcium	C1	NO OF PATIENTS	12	6	18	P value 0.782 Not significant
		% within Hypertension	27.3%	23.1%	25.7%	
	C2	NO OF PATIENTS	10	6	16	
		% within Hypertension	22.7%	23.1%	22.9%	
	C3	NO OFNTS PATIE	9	8	17	
		% within Hypertension	20.5%	30.8%	24.3%	
	C4	NO OF PATIENTS	13	6	19	
		% within Hypertension	29.5%	23.1%	27.1%	
Total		NO OF PATIENTS	44	26	70	

PATIENTS WITH DIABETES MELLITUS IN DIFFERENT CALCIUM QUARTILES

			Diabetes Mellitus		Total	
			Yes	No		
Corrected Serum Calcium	C1	NO OF PATIENTS	8	10	18	p value 0.778 Not significant
		% within Diabetes Mellitus	25.8%	25.6%	25.7%	
	C2	NO OF PATIENTS	7	9	16	
		% within Diabetes Mellitus	22.6%	23.1%	22.9%	
	C3	NO OF PATIENTS	6	11	17	
		% within Diabetes Mellitus	19.4%	28.2%	24.3%	
	C4	NO OF PATIENTS	10	9	19	
		% within Diabetes Mellitus	32.3%	23.1%	27.1%	
Total		NO OF PATIENTS	31	39	70	

PATIENTS WITH HYPERTENSION IN DIFFERENT ALBUMIN QUARTILES

			Hypertension		Total	
			Yes	No		
Serum Albumin	A1	NO OF PATIENTS	13	7	20	p value 0.489 Not significant
		% within Hypertension	29.5%	26.9%	28.6%	
	A2	NO OF PATIENTS	11	6	17	
		% within Hypertension	25.0%	23.1%	24.3%	
	A3	NO OF PATIENTS	7	8	15	
		% within Hypertension	15.9%	30.8%	21.4%	
	A4	NO OF PATIENTS	13	5	18	
		% within Hypertension	29.5%	19.2%	25.7%	
Total		NO OF PATIENTS	44	26	70	

PATIENTS WITH DIABETES MELLITUS IN DIFFERENT ALBUMIN QUARTILES

			Diabetes Mellitus		Total	
			Yes	No		
Serum Albumin	A1	NO OF PATIENTS	9	11	20	p value 0.841 Not significant
		% within Diabetes Mellitus	29.0%	28.2%	28.6%	
	A2	NO OF PATIENTS	6	11	17	
		% within Diabetes Mellitus	19.4%	28.2%	24.3%	
	A3	NO OF PATIENTS	7	8	15	
		% within Diabetes Mellitus	22.6%	20.5%	21.4%	
	A4	NO OF PATIENTS	9	9	18	
		% within Diabetes Mellitus	29.0%	23.1%	25.7%	
Total		NO OF PATIENTS	31	39	70	

CALCIUM QUARTILE DISTRIBUTION ACCORDING TO NIHSS

			NIHSS				Total	
			Minor (0-4)	Moderate (5-15)	Moderate severe (16-20)	Severe (21-42)		
Corrected Serum Calcium	C1	NO OF PATIENTS	0	4	6	8	18	p value <0.001 Highly significant
		% within NIHSS	.0%	22.2%	46.2%	57.1%	25.7%	
	C2	NO OF PATIENTS	3	4	6	3	16	
		% within NIHSS	12.0%	22.2%	46.2%	21.4%	22.9%	
	C3	NO OF PATIENTS	12	3	1	1	17	
		% within NIHSS	48.0%	16.7%	7.7%	7.1%	24.3%	
	C4	NO OF PATIENTS	10	7	0	2	19	
		% within NIHSS	40.0%	38.9%	.0%	14.3%	27.1%	
Total		NO OF PATIENTS	25	18	13	14	70	

ALBUMIN QUARTILE DISTRIBUTION ACCORDING TO NIHSS

			NIHSS				Total	
			Minor (0-4)	Moderate (5-15)	Moderate severe (16-20)	Severe (21-42)		
Serum Albumin	A1	NO OF PATIENTS	0	5	6	9	20	p value <0.001 Highly significant
		% within NIHSS	.0%	27.8%	46.2%	64.3%	28.6 %	
	A2	NO OF PATIENTS	5	3	6	3	17	
		% within NIHSS	20.0%	16.7%	46.2%	21.4%	24.3 %	
	A3	NO OF PATIENTS	11	3	1	0	15	
		% within NIHSS	44.0%	16.7%	7.7%	.0%	21.4 %	
	A4	NO OF PATIENTS	9	7	0	2	18	
		% within NIHSS	36.0%	38.9%	.0%	14.3%	25.7 %	
Total		NO OF PATIENTS	25	18	13	14	70	

CALCIUM QUARTILE DISTRIBUTION ACCORDING TO MODIFIED RANKIN SCALE

CORRECTED SERUM CALCIUM		Modified Ranking scale						Total	
		1	2	3	4	5	6		
C1	NO OF PATIENTS	0	1	2	4	5	6	18	p value 0.001 Highly significant
	% within Modified Ranking scale	.0%	5.9%	20.0%	50.0%	45.5%	75.0%	25.7%	
C2	NO OF PATIENTS	2	4	1	2	5	2	16	
	% within Modified Ranking scale	12.5 %	23.5%	10.0%	25.0%	45.5%	25.0%	22.9%	
C3	NO OF PATIENTS	6	5	4	1	1	0	17	
	% within Modified Ranking scale	37.5 %	29.4%	40.0%	12.5%	9.1%	.0%	24.3%	
C4	NO OF PATIENTS	8	7	3	1	0	0	19	
	% within Modified Ranking scale	50.0 %	41.2%	30.0%	12.5%	.0%	.0%	27.1%	
TOTAL	NO OF PATIENTS	16	17	10	8	11	8	70	

ALBUMIN QUARTILE DISTRIBUTION ACCORDING TO

MODIFIED RANKIN SCALE

SERUM ALBUMIN		Modified Ranking scale						Total	
		1	2	3	4	5	6		
A1	NO OF PATIENTS	0	2	2	4	6	6	20	p value 0.002 Highly significant
	% within Modified Ranking scale	.0%	11.8%	20.0%	50.0%	54.5%	75.0%	28.6%	
A2	NO OF PATIENTS	4	3	1	2	5	2	17	
	% within Modified Ranking scale	25.0%	17.6%	10.0%	25.0%	45.5%	25.0%	24.3%	
A3	NO OF PATIENTS	5	5	4	1	0	0	15	
	% within Modified Ranking scale	31.3%	29.4%	40.0%	12.5%	.0%	.0%	21.4%	
A4	NO OFPATIENTS	7	7	3	1	0	0	18	
	% within Modified Ranking scale	43.8%	41.2%	30.0%	12.5%	.0%	.0%	25.7%	
TOTAL	NO OF PATIENTS	16	17	10	8	11	8	70	

RESULTS

AGE DISTRIBUTION

In our study, mean age group is 48.84 years. About 17% of patients are below age 40.About 31% of patients are between age 41-50.About 51% of patients are between 51-60.

SEX DISTRIBUTION

In our study, about 61.4% are male and about 38.6% are about female.

NIHSS DISTRIBUTION

About 35.7% belong to NIHSS grade minor.

About 25.7% of patients belong to moderate.

About 18.6% of patients are moderate severe.

About 20% belong to severe group.

MRS DISTRIBUTION

In our study,about 22.9% belong to MRS 1.About 24.3% belong to MRS 2.About 14.3%-MRS 3.About 11.4% belong to MRS 4. About 15.7% belong to MRS 5.About 11.4% of patients belong to MRS 6.

CORRECTED SERUM CALCIUM DISTRIBUTION

In this study, about 25.7% patients have serum calcium value of C1(<=8.59).About 22.9% have serum calcium C2(8.60-8.99).About 24.3% of patients have serum Calcium value of C3(9.0-9.39).About 27.1% have serum calcium of about C4(>9.40)

SERUM ALBUMIN DISTRIBUTION

About 28.6% of patients have serum Albumin value of A1(<3.49).About 24.3% have serum Albumin A2(3.50-3.99). About 21.4% of patients have serum Albumin value of A3(4.00-4.49).About 25.7% have serum Albumin of about A4(>4.5).

CORRELATION OF AGE AND SEX WITH DIFFERENT CALCIUM AND ALBUMIN QUARTILES

In our study, we analysed the age with different calcium and albumin quartiles and p value obtained was insignificant. Sex distribution was analysed with different calcium and albumin quartiles and p value was insignificant. This shows age and sex has no influence over different calcium and albumin quartiles in our study.

DISTRIBUTION OF PATIENTS WITH HYPERTENSION ON DIFFERENT CALCIUM AND ALBUMIN QUARTILES

In our study, we analysed the distribution of hypertensive patients on calcium and albumin quartiles to find out any significant association of hypertension in different calcium and albumin quartiles .

p value is about 0.782 which is not significant (hypertension on different calcium quartiles) and p value is about 0.489 ,not significant (hypertension on different albumin quartiles).This shows there is no significant association between hypertension on various calcium and albumin quartiles.

DISTRIBUTION OF PATIENTS WITH DIABETES MELLITUS ON DIFFERENT CALCIUM AND ALBUMIN QUARTILES

p value is about 0.778 which is not significant (DM on different calcium quartiles).

p value is0.841 , not significant (DM on different albumin quartiles).This shows Diabetes mellitus does not influence the different calcium and albumin quartiles.

CORRELATION BETWEEN CORRECTED SERUM CALCIUM AND NIHSS AND MODIFIED RANKIN SCALE

In our study, p value between corrected serum calcium and NIHSS is <0.001 which is highly significant.

p value between corrected serum calcium and modified rankin scale is 0.001 which is highly significant.

This shows that lower corrected serum calcium is associated with poor prognosis in acute ischemic stroke as indicated by higher scores of NIHSS and MRS and higher levels are associated with good outcome.

CORRELATION BETWEEN SERUM ALBUMIN AND NIHSS, MODIFIED RANKIN SCALE

In our study, p value between serum albumin and NIHSS is <0.001, highly significant. p value between serum albumin and MRS is 0.002 which is highly significant.

This shows significant association between them. Higher values of serum albumin is associated with good outcome in acute ischemic stroke as indicated by NIHSS and MRS and lower values associated with higher severity of ischemic stroke.

DISCUSSION

DISCUSSION

In this study, 70 patients admitted with acute ischemic stroke in RGGGH, Chennai, based on inclusion, exclusion criteria were analysed. They were subjected to detailed clinical examination and severity of stroke was analysed using NIHSS and one week functional outcome was assessed using modified rankin scale. Serum calcium and serum albumin were obtained at the time of admission.

Corrected serum calcium and serum albumin were correlated with NIHSS and MRS and p value obtained was statistically significant indicating significant association between them.

SEX

In this study, among 70 patients, males are affected more. Males-61.4% females-38.6%. This was supported by Gupta A et al [26] where incidence in males is 70% and females is 30%.In a study by Sani abubakar et al male-52% and females 48%.In a study by Bruce ovbiagele et al [33]male 55% female 45%. In study by Gaurav M Kasundra et al males 58% females 42%

SAMPLE SIZE

In our study we included 70 patients.Study by Gupta A et al include 50 patients.Study by Gaurav M Kasundra et al includes 50 patients. Study by Bruce ovbiagele et al is a large study where 659 patients were subjected.

AGE

In our study mean age group is 48.84 years.In study by Gupta A et al mean age is 62 years.In study by Gaurav M kasundra mean age is 59.98+/-10.8.In study by Bruce ovbiagele et al mean age is 70+/-10.

CORRECTED SERUM CALCIUM

In our study we classified calcium quartiles as C1 <=8.59 , C2 8.60-8.99, C3 9.0-9.39, C4 >9.40.This was supported by study of Gupta A et al. In study by Bruce ovbiagele et al C1 <8.82, C2 8.83-9.18, C3 9.19-9.49, C4 >=9.50. In study by Brian H. Buck et al [34] C1 <8.7, C2 8.7-8.9, C3 9.0-9.3, C4 >9.3.

SERUM ALBUMIN

In this study albumin quartiles are A1 <3.49, A2 3.50-3.99, A3 4.00-4.49, A4 >4.5.This was supported by study of Sani Abubakar et al.

HYPERTENSION AND DIABETES WITH SERUM CALCIUM AND SERUM ALBUMIN

In our study hypertension and diabetes were correlated with corrected serum calcium and serum albumin, p value obtained was not significant indicating presence of hypertension and diabetes had no effect on calcium and albumin level in this study. This was supported by study done by Gupta A et al.

CORRECTED SERUM CALCIUM WITH NIHSS AND MRS

In our study corrected serum calcium is correlated with NIHSS and MRS, p value obtained was highly significant. This was supported by studies of Gupta A et al, Bruce ovbiagele et al, Brian H.Buck et al.

SERUM ALBUMIN WITH NIHSS AND MRS

In this study, serum albumin correlated with NIHSS and modified rankin scale, p value is highly significant. This was supported by studies of Dziedzic T et al[30], Idicula TT et al[32], Sani Abubakar et al, .Kasundra G et al[35], Cho YM et al[36].

CONCLUSION

CONCLUSION

This study shows that stroke severity and the functional outcome differ significantly with different calcium and albumin quartiles. The stroke severity is more at low calcium and low albumin level than at higher calcium and albumin level and also functional outcome in them is better when the levels of calcium and albumin are higher. The association is independent. This shows that corrected serum calcium and serum albumin can be used as a indicator of severity and for predicting prognosis in acute ischemic stroke.

LIMITATIONS

One of the limitation is sample size which is less and this study should be tested in large number of patients.

Extended follow up of patients was not possible.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Caplan CLR. Caplan's stroke: A clinical approach. 3rd Edn. New York: Butterworth Heieman; 1996.p.5-12.
2. Hatane S. Experience from Multicentre strokeregister a preliminary report. WHO 1976; 54: 541-53
3. Ropper AH, Brown RH.Editors.Cerebrovascular disease. In:Adam's and Victor's Principles of Neurology 8th edn. New York: McGraw Hill;2005.p.600-746
4. Warlow C. Stroke, transient ischemic attacks, and intracranial venous thrombosis. In: Donaghy M, Editor. Brain's diseases of the nervous system.11th edn. Newyork: Oxford university press; 2001 p.789–93.
5. Bonita R. Epidemiology of Stroke. Lancet 1992;339:342-7.
6. S.kaul et al, Thrombolysis in ischemic stroke, Medicine update 2008, ch-68, pg 520-528, vol 18, apiindia.org
7. Jeyaraj et al; Stroke epidemiology & stroke care services in India, Jurnal of Stroke, 2013: 15(3): 128-134
8. Easton JD et al: definition and evaluation of transtient ischemic attack. Stroke 40: 2276,2009
9. Oppenheimer SM. Diabetes Mellitus and early Mortality from Stroke. BMJ 1985;

10. Markus HS. Cerebral perfusion and stroke. J Neurosurg Psychiatry 2004; 75:353
11. Atkins ER, BrodieFG.Dynamicautoregulation is compromised acutely following mild ischemic stroke but not transient ischemic attack. Cerebrovasc Dis 2010;29:228
12. Aries MJ, Elting JW et al, cerebral autoregulation in stroke; review of transcranial Doppler studies. Stroke 2010; 41;2697.
13. Longo,fauci,kasper,hauser,jameson,loscalzo,harrisons principles of internal medicine,18th edition
14. Azzimondi G, Bassein L, Nonino F, et al. Fever in acute stroke worsens prognosis: a prospective study. Stroke. 1995; 26: 2040–3
15. Dalal PM. Stokes in young and elderly: risk factors and strategies for stroke prevention. J Assoc Physicians India 1997; 45: 125-31
16. Coull BM, Williams LS, Goldstein LB, et al. Anticoagulants and antiplatelet agents in acute ischemic stroke. Stroke. 2002; 33: 1934–42 85
17. International Stroke Trial Collaborative Group. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke.Lancet.1997; 349: 1569–81.

18. Adams HP, Mohr JI, Thompson JL, Lazar RM, Lewis B, Sacco RL et al. Guidelines for early management of patients with acute ischemic stroke. Stroke.2003;34:1506.
19. Menotti A, Lanti M, Seccareccia F, et al: Multivariate prediction of the first major cerebrovascular event in an Italian population sample of middle-aged men followed up for 25 years. Stroke 1993, 24: 42-48.
20. Jamrozik K, Broadhust RJ, Andeson CS, Stewart-Wynne EG: The role of lifestyle factors in the etiology of stroke: a population-based casecontrol study in perth,Western Australia. Stroke 1994, 25: 51-59.
21. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. Lancet. May 10 2008;371(9624):1612-23. [Medline].
22. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. Trends Neurosci. Sep 1999;22(9):391-7. [Medline].
23. Yuan J, Yankner BA. Apoptosis in the nervous system. Nature. Oct 12 2000;407(6805):802-9. [Medline].
24. Latchaw RE, Yonas H, Hunter GJ, Yuh WT, Ueda T, Sorensen AG, et al. Guidelines and recommendations for perfusion imaging in cerebral ischemia: A scientific statement for healthcare professionals by the writing group on perfusion imaging, from the

Council on Cardiovascular Radiology of the American Heart Association. Stroke. Apr 2003;34(4):1084-104. [Medline].

25. Bansal recent concept of stroke , Medicine update 135 -137.
26. Gupta A, Dubey U, Kumar A, Singh S. Correlation of serum calcium levels with severity and functional outcome in acute ischemic stroke patients. Int J Res Med Sci 2015;3:3698-702.
27. Siesjo B. Cerebral circulation and metabolism. J Neurosurgery. 1984 May;60(5):883-908.
28. Buck Brian H, Liebeskind David S, Saver Jeffrey L, Bang Oh Young, Starkman Sidney, Ali Latisha K, et al. Association of higher serum calcium levels with smaller infarct volumes in acute ischemic stroke. Archives of Neurology. 2007;64(9):1287-91
29. Kristian T, Siesjo BK. Calcium in ischemic cell death. Stroke 1998;29:705- 18
30. Dziedzic T, Slowik A, Szezudlik A. Serum albumin level as a predictor of ischaemic stroke outcome. Stroke. 2004;35(1):156-158.
31. Belayev L, Liu Y, Zhao W, Busto R, Ginsberg MD. Human albumin therapy of acute ischemic stroke. Marked neuroprotective efficacy at moderate doses and with a broad therapeutic window. Stroke. 2001; 32: 553–560

32. Idicula TT, Waje-Andreassen U, Brogger J, Naess H, Thomassen L. Serum albumin in ischemic stroke patients: the higher the better. The Bergen Stroke Study. Cerebrovasc Dis. 2009; 28(1): 13-7

33. Ovbiagele B, Starkman S, Teal P, Lyden P, Kasti M, Davis SM, et al. and on behalf of the Vista Investigators. Serum calcium as prognostication in ischemic stroke. Stroke. 2008;39(8):2231-6.

34. Giri S, Agarwal MP, Sharma V. Correlation of serum calcium levels with neurologic severity and short-term outcome in acute ischemic stroke. J Assoc Physicians India 2009;74:112

35. Kasundra G, Sood I. Prognostic significance of serum albumin levels in acute ischemic stroke. Natl J Integr Res Med 2014;5:1-4.

36. Cho YM, Choi IS, Bian RX, Kim JH, Han JY, Lee SG. Serum albumin at admission for prediction of functional outcome in ischemic stroke patients. Neurol Sci 2008;29:445-9

37. Appel SA, Molshatzki N, Schwammenthal Y, Merzeliak O, Toashi M, Sela BA, *et al*. Serum calcium levels and long-term mortality in patients with acute stroke. Cerebrovasc Dis 2011;31:93-9.

38. Hong SJ, Chiou GC. Effects of intracellular calcium reduction by dantrolene on prevention/treatment of ischemic stroke. J Cardiovasc Pharmacol Ther 1998;3:299-304.

39. Guven H, Cilliler AE, Koker C, Sarikaya SA, Comoglu SS. Association of serum calcium levels with clinical severity of acute ischemic stroke. Acta Neurol Belg 2011;111:45-9.
40. Belayev L, Zhao W, Pattany PM, Weaver RG, Huh PW, Lin B, Busto R, Ginsberg MD. Diffusion-weighted magnetic resonance imaging confirms marked neuroprotective efficacy of albumin therapy in focal cerebral ischemia. Stroke. 1998; 29: 2587–2599.

ANNEXURES

PROFORMA

NAME : AGE/SEX:

ADDRESS: OCCUPATION:

COMPLAINTS:

PAST HISTORY:

PERSONAL HISTORY:

TREATEMENT HISTORY:

GENERAL EXAMINATION:

VITAL SIGNS:

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN:

CNS:

GCS:

	RIGHT	LEFT
HIGHER MENTAL FUNCTIONS		
CRANIAL NERVES		

OLFACTORY OPTIC OCULOMOTOR TROCHLEAR ABDUCENT TRIGEMINAL FACIAL VESTIBULOCOCHLEAR GLOSSOPHARYNGEAL VAGUS SPINAL ACCESSORY HYPOGLOSSAL		
MOTOR		
BULK: UL LL		
TONE: UL LL		
POWER:UL LL		
REFLEX:UL LL		
PLANTAR		

SENSORY EXAMINATON:

CEREBELLAR SIGNS:

SIGNS OF MENINGEAL IRRITATION:

NIHSS SCORE:

Score	Stroke Severity
0	No Stroke Symptoms
1-4	Minor Stroke
5-15	Moderate Stroke
16-20	Moderate to Severe Stroke
21-42	Severe Stroke

MODIFIED RANKIN SCALE:

The scale runs from 0-6, running from perfect health without symptoms to death.

- 0 - No symptoms.
- 1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3 - Moderate disability. Requires some help, but able to walk unassisted.
- 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- 6 - Dead.

INVESTIGATIONS

SERUM CALCIUM

SERUM ALBUMIN

C0RRECTED CALCIUM

= SERUM CALCIUM +0.8 * (4 – SERUM ALBUMIN)

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.G.Diana
Post Graduate in M.D. General Medicine
Madras Medical College
Chennai 600 003

Dear Dr.G.Diana,

The Institutional Ethics Committee has considered your request and approved your study titled **"CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISHEMIC STROKE " - NO.04032016.**

The following members of Ethics Committee were present in the meeting hold on **01.03.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Dr.Baby Vasumathi, Director, Inst. of O&G,Ch-8	: Member
7.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3	: Member
8.Prof.Srinivasagalu,Director,Inst.of Int.Med.,MMC,Ch-3	: Member
9.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

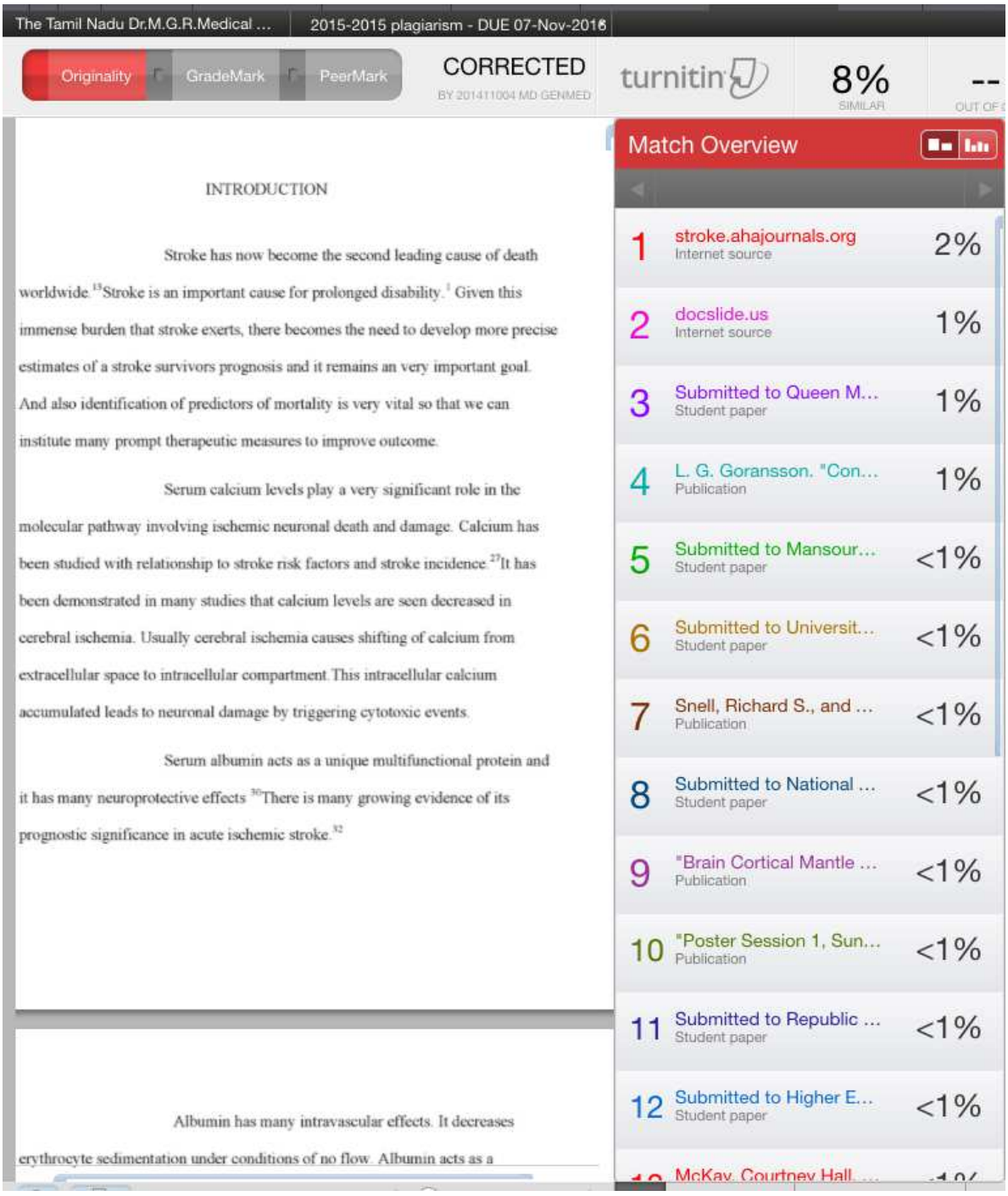
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

TURNITIN PLAGIARISM SCREEN SHOT



DIGITAL RECEIPT

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201411004 Md Genmed DIANA.G
Assignment title:	2015-2015 plagiarism
Submission title:	CORRECTED SERUM CALCIUM AN..
File name:	DIANA_THESIS_FINAL.docx
File size:	7.88M
Page count:	90
Word count:	6,390
Character count:	35,210
Submission date:	19-Sep-2016 12:38AM
Submission ID:	706947472

INTRODUCTION

INFORMATION SHEET

We are conducting a study on **"CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND THE SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE "** among patients admitted in EMERGENCY MEDICINE DEPARTMENT in Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to assess the ROLE OF CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND SHORT TERM (ONE WEEK) FUNCTIONAL OUTCOME IN ACUTE ISCHEMIC STROKE PATIENTS.

We are selecting certain cases and if you are found eligible, we may be using your blood samples to do certain tests which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment

Signature of Investigator

Signature of Participant

PATIENT CONSENT FORM

Study Detail	:	"CORRECTED SERUM CALCIUM AND SERUM ALBUMIN IN PREDICTING THE SEVERITY AND THE SHORT TERM FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE"
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from ❑

any deterioration in my health or well being or any unexpected or unusual symptoms.

e) I hereby consent to participate in this study. ❑

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required. ❑

SIGNATURE OF INVESTIGATOR IMPRESSION

SIGNATURE/THUMB

STUDY INVESTIGATOR'S NAME:

PATIENT'S NAME AND ADDRESS:

DR.G.DIANA

MASTER CHART

S.NO	AGE	SEX	HTN	DM	CORRECTED CALCIUM (mg/dl)	SERUM ALBUMIN (mg/dl)	NIHSS	MODIFIED RANKIN SCALE
1	42	MALE	YES	NO	9.6	5.1	3	1
2	40	MALE	YES	NO	8.8	3.7	18	4
3	58	FEMALE	YES	NO	9.1	3.6	36	5
4	58	MALE	YES	NO	9.22	4	11	2
5	47	MALE	NO	YES	9.11	4.2	2	1
6	48	MALE	YES	NO	7.8	3	20	5
7	38	MALE	NO	NO	8.3	3.16	10	2
8	53	MALE	NO	YES	10	4.85	4	2
9	57	MALE	YES	NO	9.82	4.65	8	2
10	51	FEMALE	NO	YES	9.57	4.6	32	4
11	47	FEMALE	YES	NO	7.9	3.1	15	5
12	53	FEMALE	YES	YES	10.1	5.2	2	1
13	46	MALE	YES	NO	9.45	4.6	30	3
14	58	MALE	YES	YES	9.7	4.9	11	2
15	46	FEMALE	YES	NO	9.87	4.98	2	1
16	58	MALE	YES	YES	8.7	3.52	30	6
17	25	FEMALE	NO	NO	9.25	3.9	4	1
18	47	MALE	NO	NO	8.64	3.64	20	5
19	51	FEMALE	NO	YES	8.9	3.74	10	2
20	53	FEMALE	YES	NO	9.3	3.92	4	1
21	54	MALE	NO	NO	9.28	4.42	3	1
22	54	FEMALE	YES	NO	8.6	3.58	31	6

23	60	MALE	NO	YES	8.72	3.5	20	5
24	47	FEMALE	YES	NO	8.87	3.9	3	1
25	42	MALE	NO	NO	8.68	3.8	12	2
26	59	FEMALE	YES	YES	8.62	3.6	17	5
27	31	MALE	NO	NO	8.84	3.96	4	2
28	50	MALE	YES	YES	8.64	3.74	16	4
29	58	FEMALE	NO	YES	8	2.6	38	6
30	49	FEMALE	NO	YES	8.98	3.2	9	2
31	53	MALE	YES	YES	7.2	2	40	6
32	54	FEMALE	NO	NO	8.3	2.84	18	4
33	47	FEMALE	YES	NO	9.92	4.92	3	2
34	38	MALE	NO	NO	9.43	5.1	7	1
35	51	MALE	YES	YES	10.12	4.97	4	2
36	38	MALE	YES	NO	9.78	4.98	4	2
37	57	MALE	YES	YES	9.47	4.72	13	3
38	26	FEMALE	NO	NO	9.18	4.46	18	4
39	47	MALE	NO	YES	9.31	4.3	10	3
40	39	MALE	YES	NO	8.9	3.88	2	1
41	60	MALE	YES	YES	7.1	2.5	36	6
42	42	MALE	YES	NO	9.2	4.24	2	1
43	42	MALE	YES	NO	8.2	2.8	30	6
44	59	MALE	YES	YES	9.14	4.08	4	3
45	54	MALE	YES	NO	8.62	3	28	5
46	44	MALE	NO	NO	8.4	3.4	8	3

47	59	MALE	YES	YES	7.5	2.9	34	6
48	50	FEMALE	YES	YES	7	2.72	40	6
49	48	FEMALE	YES	NO	9.38	4.12	4	3
50	51	FEMALE	YES	NO	8.2	2.5	28	5
51	48	MALE	NO	YES	8.2	3.1	20	4
52	53	FEMALE	YES	YES	7.8	3.2	17	5
53	52	FEMALE	YES	YES	9	4.32	3	1
54	39	MALE	NO	NO	9.32	4.1	12	3
55	53	MALE	NO	YES	9.2	4.4	3	2
56	36	MALE	YES	NO	7.9	2.8	16	4
57	40	MALE	YES	NO	8.2	3.2	10	3
58	55	MALE	NO	YES	7.3	2.9	31	5
59	47	FEMALE	YES	NO	8.1	3.1	18	4
60	58	FEMALE	YES	NO	9.3	4.12	4	2
61	55	FEMALE	YES	NO	8.78	3.6	19	5
62	51	MALE	YES	YES	9.36	4.28	3	2
63	58	MALE	YES	YES	8.94	3.84	12	3
64	28	MALE	NO	NO	9.92	4.88	2	1
65	45	FEMALE	YES	NO	9.41	4.3	14	3
66	56	FEMALE	NO	NO	9.06	4.1	3	2
67	59	MALE	YES	NO	9.53	4.82	11	2
68	43	MALE	YES	NO	9.87	4.99	6	1
69	52	FEMALE	NO	YES	10.1	4.28	4	1
70	52	MALE	NO	YES	9.67	5	1	1